Nigerian Medical Journal
NIGERIA MEDICAL ASSOCIATION
Print ISSN 0300-1652, E-ISSN 2229-774X

Original Article

Pattern of Expression of Oestrogen and Progesterone Receptors in Ovarian Carcinoma from a Tertiary Center in Nigeria: A 10-Year Retrospective Study.

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Abstract

Background: Ovarian cancer (OC) is the seventh most common malignancy among women globally and a major cause of cancer-related mortality, with approximately 239,000 new cases and 152,000 deaths each year. Despite extensive research, there is currently no effective public health screening method for early detection, as commonly used investigations such as CA-125 testing, transvaginal ultrasonography, and bimanual examination lack sufficient diagnostic accuracy. This study evaluated the patterns of oestrogen receptor (ER) and progesterone receptor (PR) expression in ovarian cancer cases in Kano State, Nigeria.

Methodology: Relevant demographic data were obtained from laboratory records. Archival formalin-fixed, paraffin-embedded tissue blocks were examined using haematoxylin and eosin staining, followed by immunohistochemical analysis for ER and PR. Tumours were classified according to histological type and grade, and receptor expression was assessed based on immunostaining. Statistical analysis was performed using SPSS, version 26.

Result: Sixty ovarian cancer cases were analysed, with patient ages ranging from 10 to 75 years (mean age 52 ± 14 years). High-grade serous carcinoma (HGSC) was the predominant histological subtype, accounting for 63.3% of cases, followed by mucinous carcinoma (15%). Endometrioid carcinoma and malignant Brenner tumour each represented 8.3% of cases, while low-grade serous carcinoma was the least common (5%). Most cases occurred in the sixth decade of life, with HGSC comprising 74% of tumours in this age group. Oestrogen receptor (ER) positivity was observed in 40% of cases, with HGSC showing the highest ER expression. In contrast, progesterone receptor (PR) positivity was low (15%), with most PR-positive cases also being HGSC.

Conclusion: OC incidence increased with age, predominantly affecting women aged 50 years and above. The relatively high ER expression and low PR expression highlight the potential role of hormone receptor profiling in guiding personalised treatment strategies for ovarian cancer in this setting.

Keywords: Ovarian carcinoma, oestrogen, progesterone

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How to Cite: Yunusa R, Gbenga SA, Gana SL, Hamza A, Muazu J, Abdullahi SA et al. Pattern of Expression of Oestrogen and Progesterone Receptors in Ovarian Carcinoma from a Tertiary Center in Nigeria: A 10-Year Retrospective Study. Niger Med J 2025; 67 (1): 2532-2541.

Quick Response Code:

https://doi.org/10.71480/nmj.v67i1.1231

Introduction

Ovarian carcinoma (OC) is a malignant epithelial tumour arising from the ovary or fallopian tube and accounts for approximately 90% of ovarian malignancies.[1-3] Globally, OC is the seventh most common cancer among women and a leading cause of gynaecological cancer mortality.[4,5] In 2022, an estimated 323,000 new cases and 207,959 deaths were recorded worldwide, with higher incidence rates in North America and Europe.[6] The global age-standardised incidence rate is 6.6 per 100,000 women.[7] OC remains the most common gynaecological cause of cancer-related death in the United States and the fifth leading cause of cancer mortality among women.[6] Although OC is less common among women of African descent, outcomes are often worse among African Americans than among Africans residing in Africa, suggesting environmental and lifestyle influences on disease patterns and prognosis.[8,9]

In developing countries, OC constitutes approximately 18.8% of gynaecological malignancies, compared with 28.7% in developed nations.[10] Nigerian studies report variable prevalence, with OC accounting for 16.3% of malignancies in Ibadan, 4.8% of all cancers in Bauchi, and 8.2% of female cancers in Kano.[11-14] OC is the second most common gynaecological cancer in Nigeria and carries the poorest prognosis, largely due to late-stage presentation (FIGO III–IV) and high mortality rates.[2,15] Owing to its insidious onset, OC has a high case-fatality rate (≈59.2%) and a 5-year survival rate of approximately 45%.[10,16]

Steroid hormones have been implicated in the aetiology and progression of OC, with several studies reporting associations between oestrogen receptor (ER) and progesterone receptor (PR) expression and improved survival outcomes.[10,17] PR expression, in particular, has been linked to a favourable prognosis in endometrioid carcinoma and high-grade serous carcinoma (HGSC), while the prognostic role of ER remains controversial.[15,17] Despite this, limited data from Nigeria describe ER and PR expression patterns in OC.

OC development has been explained by hypotheses such as Fathalla's "incessant ovulation" theory and, more recently, a dualistic model of epithelial ovarian carcinogenesis. Type I tumours are indolent, low-grade, and often arise from Müllerian-derived lesions, and they harbour mutations in genes such as KRAS, BRAF, PTEN, and ARID1A.[18] Type II tumours, including HGSC, are aggressive, genetically unstable, and originate from serous tubal intraepithelial carcinoma (STIC) lesions, frequently exhibiting TP53 mutations and BRCA1/2 dysfunction.[15,17,19,20]

Methodology

This was a 10-year retrospective study (January 2011–December 2020) conducted in the Department of Histopathology, Aminu Kano Teaching Hospital (AKTH), a major tertiary referral centre in North-western Nigeria. Ethical approval was obtained from the Aminu Kano Teaching Hospital Ethics Committee on 11 January 2023 (reference number: AKTH/MAC/SUB/12A/P-13/V1/3564).

The study population comprised all histologically confirmed cases of OC diagnosed during the study period. Of the 122 ovarian cancer cases identified, 87 were epithelial cancers, of which 60 cases met the study criteria and were included using convenience sampling. Excluded cases were those with missing or damaged tissue blocks, insufficient clinical information (particularly age), metastatic ovarian cancer, and non-epithelial ovarian cancers.

Patient age at diagnosis was retrieved from laboratory records. Original haematoxylin and eosin (H&E)-stained slides for all included cases were independently reviewed by two senior pathologists to confirm the diagnosis, classify the tumour according to the World Health Organization (WHO) Classification of Tumours of the Female Genital Tract (2020), and assign a tumour grade. Consensus was achieved in the few cases where there were discrepancies in diagnosis.

Immunohistochemistry

Immunohistochemistry (IHC) was performed on 4-µm-thick sections cut from representative FFPE tissue blocks using the UltraVision Quanto Detection System (Thermo Fisher Scientific, USA). Ready-to-use primary monoclonal antibodies against ER (clone EP1) and PR (clone PgR 1294) were applied according to the manufacturer's protocol (Dako), with heat-induced antigen retrieval in citrate buffer (pH 6.0). Normal ovarian stroma served as an internal positive control. For negative controls, the primary antibody was replaced with distilled water.

Nuclear ER and PR staining was evaluated using the Allred scoring system, which incorporates both staining intensity and the proportion of positive tumour cells. Intensity is scored from 0 to 3, and proportion from 0 to 5. The final score is the sum of the two components, ranging from 0 to 8. Scores of 0–2 were considered negative, while scores of 3–8 were considered positive. The Allred scoring system, originally validated in breast cancer, provides a standardised semi-quantitative method for assessing hormone receptor expression, with a documented correlation with tumour aggressiveness and prognosis. Because ovarian tissue exhibits hormonal responsiveness similar to breast tissue, the Allred scoring system is considered applicable and feasible for evaluating hormone receptor status in ovarian tumours. Scoring was performed independently by two senior pathologists, and consensus was reached in the four cases with discrepant scores.

Statistical analysis

Data were analysed using the Statistical Package for the Social Sciences (SPSS), version 26 (SPSS Inc., Chicago, IL, USA). Continuous variables (age) were summarised as mean and standard deviation. The chi-square test was used to assess associations between categorical variables. A p-value of < 0.05 was considered statistically significant. We acknowledge the limited statistical power due to the relatively small sample size.

Results

Within the study period, a total of 1,613 cancer diagnoses were made. Of these, 578 were gynaecological malignancies, with ovarian cancer constituting 122 cases. Eighty-seven were epithelial cancers, of which 60 cases met the study criteria. Among these 60 cases, patient ages ranged from 10 to 75 years, with a mean age of 52 ± 14.2 years. The highest frequency of cases was observed in patients in their sixth and seventh decades of life. OC was more prevalent among patients aged 50 years and older, accounting for 73.3% of the cases, compared with 26.7% in patients younger than 50 years.

High-grade serous carcinoma (HGSC) was the most common type of OC, accounting for 38 cases (63.3%), followed by mucinous carcinoma with 9 cases (15%). Endometrioid carcinoma and malignant Brenner tumour each accounted for 5 cases (8.3%), while low-grade serous carcinoma was the least frequent type, comprising 3 cases (5%).

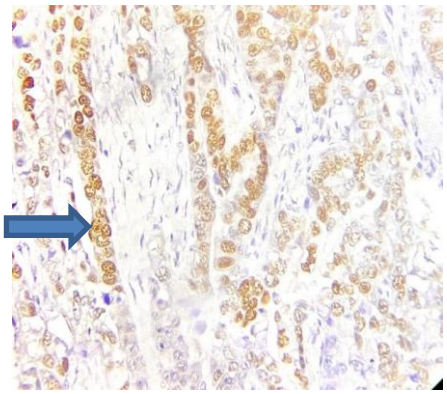

Figure 1: showing positive nuclear staining of the target antigen. ER antibody ×100 (immunoperoxidase technique. The figure shows high-grade serous carcinoma exhibiting cords and sheets of malignant epithelial cells with intense nuclear staining (arrow).

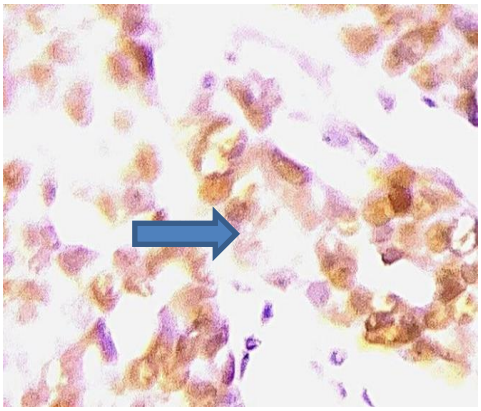

Figure 2: showing positive nuclear staining of the target antigen. PR antibody ×100 (immunoperoxidase technique. The figure shows high-grade serous carcinoma exhibiting nests of malignant epithelial cells with intense nuclear staining (arrow).

Table 1: Frequency of gynaecological cancers in Aminu Kano Teaching Hospital

Cancer type	Frequency	Percentage
Cervical cancer	339	58.7
Ovarian cancer	122	21.1
Endometrial cancer	91	15.7
Choriocarcinoma	20	3.5
Vulva	5	0.9
Vagina	1	0.2
Total	578	100

The majority of OC cases were classified as grade 3 carcinoma, with 38 cases (69%) recorded. Intermediate-grade carcinomas accounted for 14 cases (25%), and low-grade carcinomas comprised 3 cases (6%).

Of the 60 cases, 24 (40%) showed oestrogen receptor (ER) positivity, while 36 (60%) were negative for ER expression. Despite the higher frequency of ER positivity in patients aged over 50 years (79.2%), there was no statistically significant association between age and ER expression ($p = 0.569$) (Table 2, Figure 1).

Nine of the 60 cases (15%) were positive for progesterone receptor (PR), while 51 (85%) were PR negative. The association between histologic subtype and PR expression was not statistically significant ($\rho = 0.616$). Almost two-thirds of the PR-positive cases (6 cases, 66.7%) occurred in patients in their sixth and seventh decades of life; however, the relationship between age and PR expression was also not statistically significant ($\rho = 0.608$) (Table 2, Figure 2).

Table 2: Showing expression of ER and PR in various types of OC

Variable	Histologic subtypes									
	Number examined	HGSC	MC	EC	MBT	LGSC				
	n(%)	n(%)	n(%)	n(%)	n(%)	n(%)	df	χ^2	95%CI	p-value
ER										
Negative	36(60)	20(55.5)	7(19.4)	3(8.3)	4(11.1)	2(5.6)	4	2.934	2.354-3.025	0.569
Positive	24(40)	18(75)	2(8.3)	2(8.3)	1(4.2)	1(4.2)				
PR										
Negative	51(85)	31(60.8)	7(12.3)	3(5.9)	4(7.8)	2(3.9)	4	2.663	2.418-2.867	0.616
Positive	9(15)	7(77.8)	0(0)	1(11.1)	1(11.1)	0(0)				

Key: ER=Oestrogen receptor PR= Progesterone receptor, n=Number of cases, MB=Malignant Brenner Tumour LGSC= Low-grade serous carcinoma, EC= Endometrioid carcinoma MC=Mucinous carcinoma, df= Degree of freedom, χ^2= Chi-square fisher's exact test, CI= Confidence interval, %=percentage

Discussion

This study found that OC accounted for 21.1% of gynaecological malignancies, lower than prior Nigerian reports (23.6–30.5%).[14,21-29] This discrepancy may be due to differences in study duration and population characteristics. The mean age at diagnosis was 52 ± 14.2 years, with 73.3% of cases occurring in women aged ≥50 years. This is consistent with previous African studies (e.g. Sudan: 55 years; Nigeria: 54–57 years).[14,24,25] However, it differs markedly from data from developed countries, where the peak incidence of OC occurs at 75–79 years.[24,26,27] Earlier onset in Africa may reflect underlying genetic factors (e.g. BRCA polymorphisms), as well as environmental or socioeconomic influences.[28]

High-grade serous carcinoma (HGSC) was the most prevalent histologic subtype, accounting for 63.3% of cases. This exceeds the global average of 42.97% but is consistent with African trends of 50–65%.[8,29,30] Mucinous carcinoma accounted for 15% and endometrioid carcinoma for 8.3% of cases, while clear cell carcinoma was rare (<1%), in contrast to its higher prevalence in Asian populations.[29,31-33] The predominance of HGSC underscores the need for aggressive management of OC, as HGSC is known to be highly aggressive and is frequently associated with TP53 mutations and BRCA abnormalities.[34]

Grade 3 tumours comprised 69% of cases, which is in keeping with global data (72–73%) and signals a generally poor prognosis and the need for intensive therapy. [26,30,35]

ER positivity was observed in 40% of cases, aligning with Nigerian studies reporting ER positivity rates of 24.4–31.4% and with international data ranging from 32% to 77%.[]10,35,36] PR positivity (15%) was relatively uncommon and occurred predominantly in HGSC, highlighting the aggressive nature of this subtype. Although survival outcomes were not evaluated in this study, previous work has demonstrated that PR expression is associated with improved survival.[10,35,36] A study from Ibadan (90 OC cases) reported 33.3% PR positivity, with higher expression in grade 3 (poorly differentiated) tumours (60% of PR-positive cases) and in advanced FIGO stages (63.3% of PR-positive cases).[10] A multicentre Nigerian analysis found no significant association between PR status and survival or stage, despite generally low overall survival rates.[36]

Only 5% of cases co-expressed ER and PR, indicating that dual positivity is rare. The low rate of dual positivity may suggest distinct biological pathways influencing tumour behaviour according to hormone receptor status and may support the need for alternative therapeutic strategies beyond conventional endocrine therapy. Dual ER/PR negativity contributes to triple-negativeOC phenotypes, which are typically more aggressive.[10]

Conclusion:

This study found that the incidence of OC increases with age, predominantly affecting women over 50 years, with a mean age at diagnosis of 52 years—consistent with global epidemiological patterns. HGSC emerged as the most frequent histologic subtype, reflecting its aggressive behaviour and alignment with worldwide trends. The predominance of high-grade tumours underscores the need for intensive therapeutic strategies and timely, optimized clinical management.

Hormone receptor analysis revealed heterogeneous expression, with a substantial proportion of cases being oestrogen receptor (ER)-negative, while HGSC demonstrated the highest ER positivity. Progesterone receptor (PR) expression was infrequent and occurred predominantly in HGSC. These findings have potential implications for hormonal therapy responsiveness, particularly in ER/PR-positive subgroups.

This study underscores the importance of age-specific vigilance and subtype-tailored management in OC. Further research is warranted to elucidate the prognostic and therapeutic significance of hormone receptor status in African populations.

Limitations

The limitations of this study include its retrospective, single-centre design, the relatively small sample size, and the absence of survival or treatment response data, as well as the lack of molecular profiling (e.g. BRCA status).

Recommendations

Age-specific vigilance is recommended, with particular focus on women aged ≥50 years, although the earlier onset of OC in African populations also warrants attention in younger age groups. The high

prevalence of HGSC highlights the need for targeted therapeutic approaches, such as PARP inhibitors for BRCA-associated cases. ER/PR status may help guide hormonal therapy (e.g. aromatase inhibitors), but this requires further validation in African cohorts. In addition, multicentre studies with larger sample sizes are recommended to enhance statistical power and improve the generalisability of findings.

Acknowledgement
The authors acknowledge the support of the management of the Federal University of Health Sciences, Azare, Bauchi State.

Funding
This research was funded by the TETFUND with reference number:
TETF/DR&D/CE/UNT/AZARE/IBR/2023/VOLI.

Conflict of interest
The authors declare that there is no conflict of interest.

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