

Original Research Article

PROPORTION AND CLINICOPATHOLOGICAL CHARACTERISTICS OF TRIPLE-NEGATIVE EPITHELIAL OVARIAN CARCINOMA: A CROSS-SECTIONAL STUDY FROM A TERTIARY CARE CENTER IN SOUTH INDIA

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ABSTRACT

Background: Triple-negative epithelial ovarian carcinoma (TNEOC), characterized by negative expression of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER2), has emerged as a potential aggressive subtype of epithelial ovarian carcinoma (EOC). Limited data are available regarding its prevalence and clinicopathological characteristics in the Indian population.

Materials and Methods: This cross-sectional descriptive study was conducted among 84 women with histologically confirmed epithelial ovarian carcinoma undergoing cytoreductive surgery at a tertiary care center in South India. Clinical, radiological, surgical, and histopathological data were collected. Immunohistochemical analysis for ER, PR, and HER2 expression was performed, and tumors negative for all three markers were categorized as TNEOC.

Results: The mean age of the study population was 52.8 ± 9.9 years, and 64.3% of patients were postmenopausal. Advanced-stage disease (FIGO stage III–IV) was observed in 59.5% of cases, while high-grade tumors constituted 88.1% of the study population. Serous papillary cystadenocarcinoma was the predominant histological subtype (75%). Triple-negative epithelial ovarian carcinoma was identified in 5 patients, accounting for 6% of epithelial ovarian malignancies. Most women with TNEOC presented with advanced-stage disease and high-grade histology. Optimal cytoreduction was achieved in 85.7% of patients.

Conclusion: Triple-negative epithelial ovarian carcinoma constituted a relatively uncommon subgroup of epithelial ovarian malignancies in the present study. Despite its low prevalence, TNEOC demonstrated predominantly advanced-stage and high-grade disease. Larger multicentric studies with molecular characterization and long-term follow-up are required to better define the prognostic significance and therapeutic implications of TNEOC.

Keywords: Epithelial ovarian carcinoma; Triple-negative ovarian cancer; Estrogen receptor; Progesterone receptor; HER2; Immunohistochemistry.

INTRODUCTION

Ovarian cancer remains one of the most lethal gynecological malignancies worldwide and continues to pose a major challenge because of its asymptomatic progression and delayed diagnosis. Despite accounting for a relatively smaller proportion of female cancers, it contributes disproportionately to cancer-related mortality among women owing to its aggressive biological behavior and high recurrence rates.^[1] Globally, epithelial ovarian carcinoma (EOC) constitutes nearly 90% of all ovarian malignancies and is frequently diagnosed at an advanced stage, resulting in poor long-term survival outcomes.^[2] The overall prognosis of EOC is strongly influenced by stage at diagnosis, histological subtype, tumor grade, and response to treatment. Although advances in cytoreductive surgery and platinum-based chemotherapy have improved clinical outcomes over the past decades, recurrence and chemoresistance continue to remain significant therapeutic obstacles.^[3]

Epithelial ovarian carcinoma is a heterogeneous disease comprising multiple histopathological and molecular subtypes with variable clinical behavior and therapeutic response. High-grade serous carcinoma represents the predominant subtype and is commonly associated with advanced-stage disease and unfavorable prognosis.^[4] Conventional prognostic assessment based solely on histology and staging has several limitations in predicting disease aggressiveness and treatment response. Consequently, there has been growing interest in identifying molecular and hormonal biomarkers that may aid in risk stratification and individualized therapeutic planning.^[5]

Hormone receptor expression has emerged as an important area of research in ovarian carcinoma, particularly estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER2). These biomarkers have been extensively studied in breast carcinoma, where their expression status significantly influences prognosis and targeted therapy selection.^[6] In recent years, attempts have been made to extrapolate similar molecular classifications to ovarian malignancies. Triple-negative epithelial ovarian carcinoma (TNEOC), characterized by the absence of ER, PR, and HER2 expression, has been proposed as a distinct subtype associated with aggressive tumor biology, higher proliferative activity, poor differentiation, and adverse clinical outcomes.^[7]

Available literature regarding the prevalence and clinicopathological characteristics of TNEOC remains limited and inconsistent, particularly within the Indian population. Most existing studies originate from Western or East Asian cohorts, and the reported prevalence of TNEOC varies considerably across populations.^[7] Furthermore, data evaluating the association between triple-negative status and tumor stage, histological subtype, cytoreductive outcomes,

and clinicopathological parameters in Indian women are scarce. In this context, the present study was undertaken to determine the proportion of triple-negative epithelial ovarian carcinoma and to assess its clinicopathological characteristics among women undergoing cytoreductive surgery at a tertiary care center in South India.

MATERIALS AND METHODS

Study Design and Setting

This cross-sectional descriptive study was conducted in the Department of Obstetrics and Gynecology at Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, a tertiary care referral center in South India. The study was carried out after obtaining approval from the Institutional Ethics Committee, and written informed consent was obtained from all participants prior to enrollment.^[8]

Study Population

Women aged more than 18 years undergoing cytoreductive surgery for histologically confirmed epithelial ovarian carcinoma during the study period were included in the study. Patients with secondary metastatic ovarian malignancies involving the ovary were excluded.

Sample Size and Sampling Technique

The sample size was calculated based on the previously reported prevalence of triple-negative epithelial ovarian carcinoma.^[9] Considering an expected prevalence of 42.2%, relative precision of 25%, and confidence interval of 95%, the minimum required sample size was estimated to be 84 participants. Consecutive sampling technique was employed, and all eligible patients presenting during the study period were included.

Clinical and Radiological Evaluation

Detailed demographic and clinical information including age, parity, menopausal status, body mass index, family history of malignancy, and associated risk factors for ovarian carcinoma were recorded. Baseline biochemical investigations including serum CA-125 and carcinoembryonic antigen (CEA) levels were obtained in all patients. Radiological staging was performed using contrast-enhanced computed tomography of the abdomen and pelvis, especially in patients planned for interval cytoreductive surgery following neoadjuvant chemotherapy.^[10]

Surgical Management

All patients underwent either primary cytoreductive surgery or interval cytoreduction depending on disease operability and clinical assessment. Surgical procedures included total abdominal hysterectomy with bilateral salpingo-oophorectomy, total omentectomy, retroperitoneal lymph node dissection, bowel surgeries, and additional debulking procedures when indicated. The extent of cytoreduction was categorized according to Gynecologic Oncology Group criteria into R0 (no macroscopic residual

disease), R1 (residual disease <10 mm), and R2 (residual disease ≥10 mm).^[11]

Histopathological Examination

Resected specimens were fixed in formalin and subjected to histopathological evaluation in the Department of Pathology. Histological subtype and tumor grade were classified according to the World Health Organization classification of ovarian tumors.^[12]

Immunohistochemistry

Immunohistochemical analysis for estrogen receptor (ER), progesterone receptor (PR), and HER2 expression was performed using standardized laboratory protocols. ER and PR expression were assessed using the H-score method, while HER2 expression was interpreted according to the College of American Pathologists guidelines.^[13] Tumors showing negative expression for ER, PR, and HER2 were categorized as triple-negative epithelial ovarian carcinoma.

Outcome Measures

The primary outcome of the study was to determine the proportion of triple-negative epithelial ovarian carcinoma among women with epithelial ovarian malignancy. Secondary outcomes included evaluation of clinicopathological characteristics such as stage of disease, histological subtype, tumor grade, cytoreduction status, and tumor marker profile.

Statistical Analysis

Data were entered in Microsoft Excel and analyzed using SPSS software version 24.0 (IBM Corp., Armonk, NY, USA). Continuous variables such as age, BMI, CA-125, and CEA levels were expressed as mean ± standard deviation or median with range based on data distribution. Categorical variables including menopausal status, stage of disease, histological subtype, tumor grade, cytoreduction status, and hormone receptor expression were expressed as frequencies and percentages. Comparison between TNEOC and non-TNEOC groups was performed using Chi-square test or Fisher's exact test for categorical variables and independent sample t-test or Mann-Whitney U test for continuous variables, as appropriate. A p-value <0.05 was considered statistically significant. Due to the low number of TNEOC cases, the analysis was primarily descriptive.

RESULTS

Patient Characteristics

During the study period, 84 women with histologically confirmed epithelial ovarian carcinoma who underwent cytoreductive surgery were included in the analysis. The age of the patients ranged from 30 to 78 years, with a mean age of 52.8 ± 9.9 years. The highest proportion of patients belonged to the 51–60-year age group. Most women were multiparous, and the mean age at menarche was 13.4 ± 1.2 years. Postmenopausal women constituted

64.3% of the study population, whereas 35.7% were premenopausal (Figure 1).

The mean body mass index was 21.4 ± 2.4 kg/m², and the majority of patients belonged to the normal BMI category. Prior tubectomy was documented in 51.2% of women. Hypertension and diabetes mellitus were present in 29.8% and 19.0% of patients, respectively. Family history of malignancy was uncommon and was observed in only three patients. Endometriosis and prior ovulation induction were identified in 3.6% and 1.2% of women, respectively. The baseline demographic and clinical characteristics of the study population are summarized in Table 1.

Tumor Marker and Surgical Characteristics

The mean serum CA-125 level was 724 ± 1190.3 IU/mL. More than half of the patients demonstrated CA-125 levels greater than 200 IU/mL at presentation. The mean serum carcinoembryonic antigen (CEA) level was 2.9 ± 8 ng/mL, and elevated CEA levels (>3 ng/mL) were observed in 15.5% of patients. Tumor marker profiles are presented in Table 2.

Among the study population, 54.8% of women received neoadjuvant chemotherapy followed by interval cytoreductive surgery, whereas the remaining patients underwent primary cytoreductive surgery. The mean number of neoadjuvant chemotherapy cycles administered prior to surgery was 3 ± 2.0.

Total abdominal hysterectomy with bilateral salpingo-oophorectomy along with total omentectomy was the most commonly performed surgical procedure. Additional procedures including retroperitoneal lymph node dissection, bowel resection, splenectomy, pelvic peritonectomy, and liver surface excision were performed in selected patients with advanced disease.

Optimal cytoreduction was achieved in 85.7% of patients. Complete macroscopic resection (R0) constituted the predominant cytoreduction outcome, while residual disease ≥10 mm (R2) was observed in a smaller proportion of patients. Surgical characteristics and cytoreduction outcomes are detailed in Table 2.

Histopathological Characteristics

Histopathological examination revealed advanced-stage disease (FIGO stage III–IV) in 59.5% of patients (Figure 2). Stage IIIC disease represented the most common stage at final diagnosis. Early-stage disease (FIGO stage I–II) was observed in the remaining patients.

Serous papillary cystadenocarcinoma was the predominant histological subtype and accounted for 75% of tumors. Mucinous cystadenocarcinoma and endometrioid carcinoma each constituted 9.5% of cases, whereas clear cell carcinoma and transitional cell carcinoma were identified less frequently. Histopathological characteristics are summarized in Table 3.

Tumor grading demonstrated a predominance of high-grade tumors, which constituted 88.1% of the study population. Only a minority of tumors were

categorized as low-grade or intermediate-grade lesions.

Representative radiological, intraoperative, and histopathological findings are shown in Figures 3–5. Contrast-enhanced computed tomography demonstrated bilateral ovarian masses in patients with advanced disease (Figure 3). Intraoperative assessment revealed extensive peritoneal tumor deposits and intraperitoneal disease spread (Figure 4). Histopathological examination demonstrated features consistent with high-grade serous papillary adenocarcinoma of the ovary (Figure 5).

Hormone Receptor Expression Status

Immunohistochemical analysis demonstrated triple-negative epithelial ovarian carcinoma in 5 patients, corresponding to a prevalence of 6% within the study population (Figure 6). The remaining tumors were categorized as non-triple-negative epithelial ovarian

carcinomas. Hormone receptor expression profiles are summarized in Table 4.

The mean age of women with TNEOC was 49.4 ± 16.1 years. Most patients in the TNEOC group presented with advanced-stage disease, and all tumors demonstrated high-grade histology. Serous papillary cystadenocarcinoma remained the predominant histological subtype among both TNEOC and non-TNEOC groups.

Suboptimal cytoreduction appeared more frequent among women with TNEOC when compared with non-triple-negative tumors. Similarly, advanced-stage presentation was more commonly observed in the TNEOC group. However, due to the limited number of triple-negative cases, statistical comparison between groups was restricted. Comparative clinicopathological characteristics of TNEOC and non-TNEOC groups are presented in Table 5.

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants

Variable	Frequency (%) / Mean \pm SD
Age (years)	52.8 \pm 9.9
Age group 31–40 years	8 (9.5)
Age group 41–50 years	24 (28.6)
Age group 51–60 years	36 (42.9)
Age group >60 years	16 (19.0)
Postmenopausal status	54 (64.3)
Premenopausal status	30 (35.7)
Multiparity (≥ 2)	67 (79.7)
Prior tubectomy	43 (51.2)
Body mass index (kg/m ²)	21.4 \pm 2.4
Diabetes mellitus	16 (19.0)
Hypertension	25 (29.8)
Family history of malignancy	3 (3.6)
Endometriosis	3 (3.6)
Prior ovulation induction	1 (1.2)

Table 2: Tumor Marker Profile and Surgical Characteristics

Variable	Frequency (%) / Mean \pm SD
Serum CA-125 (IU/mL)	724 \pm 1190.3
Serum CEA (ng/mL)	2.9 \pm 8
CA-125 >200 IU/mL	46 (54.8)
Elevated CEA (>3 ng/mL)	13 (15.5)
Primary cytoreduction	38 (45.2)
Interval cytoreduction	46 (54.8)
Number of NACT cycles	3 \pm 2.0
Optimal cytoreduction	72 (85.7)
Suboptimal cytoreduction	12 (14.3)
R0 cytoreduction	58 (69.0)
R1 cytoreduction	14 (16.7)
R2 cytoreduction	12 (14.3)

Table 3: Histopathological Characteristics of Epithelial Ovarian Carcinoma

Variable	Frequency (%)
FIGO Stage I	14 (16.7)
FIGO Stage II	20 (23.8)
FIGO Stage III	42 (50.0)
FIGO Stage IV	8 (9.5)
Serous papillary cystadenocarcinoma	63 (75.0)
Mucinous cystadenocarcinoma	8 (9.5)
Endometrioid carcinoma	8 (9.5)
Clear cell carcinoma	3 (3.6)
Transitional cell carcinoma	2 (2.4)
High-grade tumors	74 (88.1)
Low/intermediate-grade tumors	10 (11.9)

Table 4: Hormone Receptor Expression Status Among Study Population

Variable	Frequency (%)
Triple-negative epithelial ovarian carcinoma	5 (6.0)
Non-triple-negative epithelial ovarian carcinoma	79 (94.0)

Table 5: Comparison Between TNEOC and Non-TNEOC Groups

Variable	TNEOC (n=5)	Non-TNEOC (n=79)
Mean age (years)	49.4 ± 16.1	53.0 ± 9.5
Advanced-stage disease (FIGO III-IV)	4 (80.0)	46 (58.2)
High-grade tumors	5 (100)	69 (87.3)
Serous histology	4 (80.0)	59 (74.7)
Optimal cytoreduction	3 (60.0)	69 (87.3)
Suboptimal cytoreduction	2 (40.0)	10 (12.7)

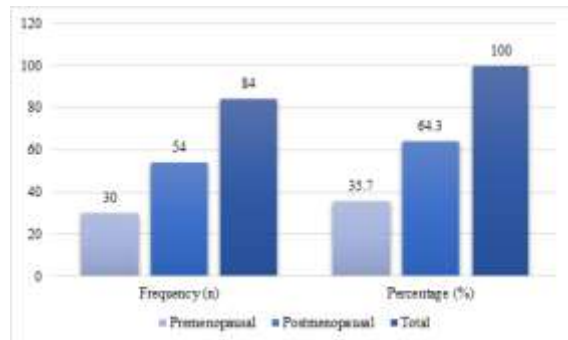


Figure 1: Distribution of Menopausal Status Among Study Population

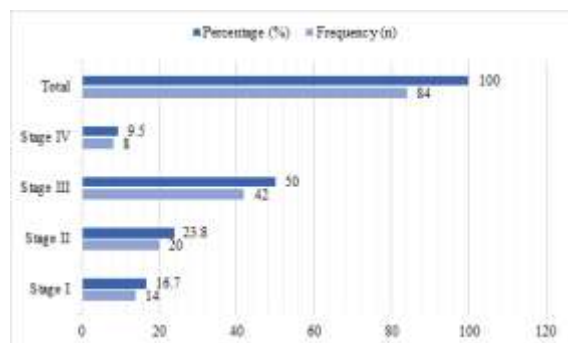


Figure 2: Distribution of FIGO Stage Among Women with Epithelial Ovarian Carcinoma



Figure 3: Contrast-Enhanced Computed Tomography Showing Bilateral Ovarian Mass

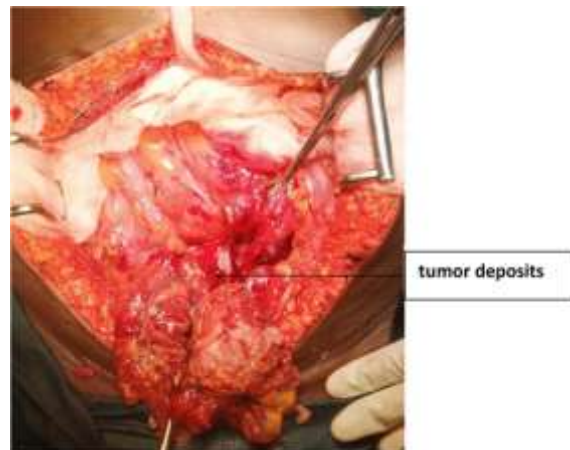


Figure 4: Intraoperative Image Showing Peritoneal Tumor Deposits

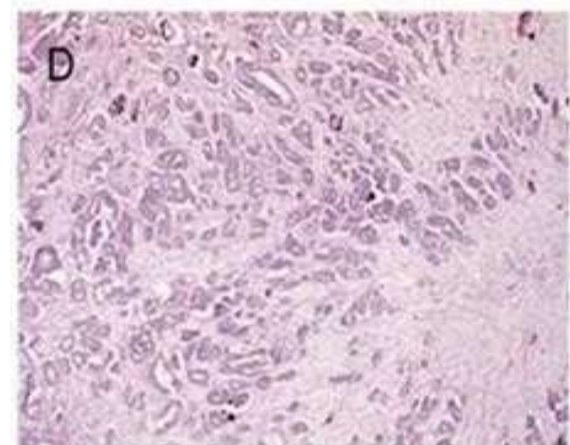
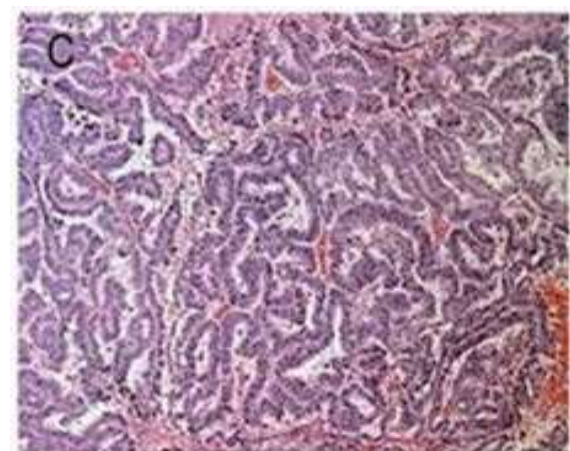


Figure 5: Histopathological Features of High-Grade Serous Papillary Adenocarcinoma

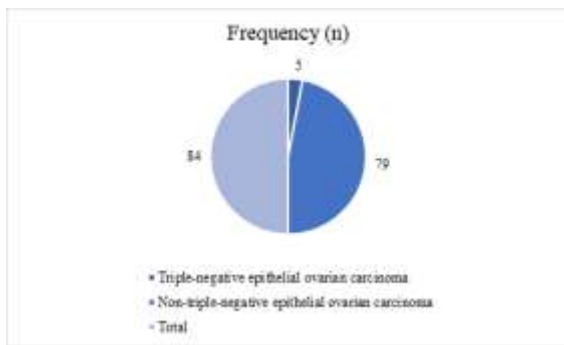


Figure 6: Hormone Receptor Expression Status Among Study Population

DISCUSSION

The present study evaluated the proportion and clinicopathological characteristics of triple-negative epithelial ovarian carcinoma among women undergoing cytoreductive surgery at a tertiary care center in South India. Triple-negative epithelial ovarian carcinoma was identified in 6% of cases, indicating that this phenotype represents a relatively uncommon subgroup of epithelial ovarian malignancies. Most patients presented with advanced-stage disease and high-grade tumors, with serous papillary cystadenocarcinoma being the predominant histological subtype. These findings are consistent with the known clinicopathological profile of epithelial ovarian carcinoma, which is frequently diagnosed at an advanced stage due to nonspecific clinical presentation.^[13]

The mean age of patients in the present study was comparable to previously published Indian and international studies on epithelial ovarian carcinoma.^[14] The majority of women were postmenopausal, which is in agreement with the recognized epidemiological pattern of ovarian malignancy.^[15]

Advanced-stage disease constituted the majority of cases in the present study, similar to earlier reports where most women presented in FIGO stage III or IV at diagnosis.^[16] Delayed diagnosis remains an important factor contributing to poor survival outcomes in ovarian cancer. Serous papillary cystadenocarcinoma was the predominant histological subtype observed, consistent with previous studies identifying high-grade serous carcinoma as the most common epithelial ovarian malignancy worldwide.^[17]

The prevalence of triple-negative epithelial ovarian carcinoma observed in the present study was lower than that reported in certain earlier studies.^[18] Variations in prevalence across studies may be related to differences in ethnicity, sample size, immunohistochemical methods, and scoring systems. Despite the low prevalence, most TNEOC cases in the present study demonstrated advanced-stage disease and high-grade histology, findings that are comparable with previous reports describing

aggressive clinicopathological behavior among triple-negative tumors.

Optimal cytoreduction was achieved in the majority of patients. Complete macroscopic resection remains an important prognostic factor in epithelial ovarian carcinoma and is associated with improved treatment outcomes.^[19] Although suboptimal cytoreduction appeared more frequent among women with TNEOC, meaningful statistical comparison was limited by the small number of triple-negative cases.

The present study provides regional data regarding triple-negative epithelial ovarian carcinoma from a tertiary care center in South India. However, the relatively small sample size and low prevalence of TNEOC limited detailed comparative analysis. In addition, long-term survival outcomes and molecular profiling were not assessed. Larger multicentric studies with extended follow-up and molecular characterization are required to better understand the biological behavior and prognostic significance of TNEOC in epithelial ovarian carcinoma.

CONCLUSION

Triple-negative epithelial ovarian carcinoma constituted a relatively small proportion of epithelial ovarian malignancies in the present study, accounting for 6% of cases. The majority of patients with epithelial ovarian carcinoma presented with advanced-stage disease and high-grade tumors, with serous papillary cystadenocarcinoma being the predominant histological subtype. Similarly, most women with triple-negative tumors demonstrated advanced-stage presentation and high-grade histology.

The findings of the present study suggest that triple-negative epithelial ovarian carcinoma may represent a clinically aggressive subgroup of ovarian malignancy. Although the low prevalence of TNEOC limited detailed statistical comparison, the observed clinicopathological profile indicates a possible association between triple-negative status and adverse tumor characteristics. Hormone receptor profiling using ER, PR, and HER2 immunohistochemistry may therefore provide additional information regarding tumor biology in epithelial ovarian carcinoma.

Optimal cytoreduction was achieved in the majority of patients, emphasizing the importance of aggressive surgical management in improving treatment outcomes in ovarian cancer. However, the biological behavior and prognostic implications of TNEOC remain incompletely understood.

The present study contributes important regional data regarding triple-negative epithelial ovarian carcinoma from a South Indian tertiary care population. Further large-scale multicentric studies with long-term follow-up, survival analysis, and molecular characterization are required to better define the prognostic significance and therapeutic implications of TNEOC. Improved understanding of

the molecular profile of these tumors may facilitate development of individualized treatment strategies and future targeted therapies in epithelial ovarian carcinoma.

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