Received: 26 February 2022 | Revised: 10 June 2022 | Accepted: 23 June 2022

DOI: 10.1002/hsr2.717

ORIGINAL RESEARCH

Health Science Reports Open Access WILEY

Predictors of early mortality risk in patients with epithelial ovarian cancer

Kehinde S. Okunade[1,2] | Sarah John-Olabode[3] | Ephraim O. Ohazurike[2] | Adaiah Soibi-Harry[2] | Benedetto Osunwusi[2] | Rose I. Anorlu[1,2]

[1]Oncology and Pathological Studies (OPS) Unit, Department of Obstetrics and Gynaecology, University of Lagos College of Medicine, Lagos, Nigeria

[2]Department of Obstetrics and Gynaecology, Lagos University Teaching Hospital, Lagos, Nigeria

[3]Department of Haematology and Blood Transfusion, University of Lagos College of Medicine, Lagos, Nigeria

Correspondence

Kehinde Sharafadeen Okunade, Department of Obstetrics and Gynaecology, College of Medicine, University of Lagos and Lagos University Teaching Hospital, Lagos, Nigeria.
Email: sokunade@unilag.edu.ng

Funding information

Fogarty International Center, Grant/Award Numbers: D43TW010134, D43TW010543, D43TW010934

Abstract

Background: To improve the overall survival of epithelial ovarian cancer (EOC) patients, a more precise risk identification after completion of standard treatment will enhance patients' follow-up surveillance and the use of individualized targeted therapy.

Aim: This study explored the potential risk predictors of early mortality in EOC patients who had standard treatment with debulking surgery and chemotherapy.

Methods: The study included 93 EOC patients who had standard treatment and were followed up between January 2011 and December 2020. The sociodemographic, clinical, and laboratory data of patients with EOC including the update on their 3-year follow-up status were retrospectively collected and analyzed. Early mortality is defined as the death of a patient within 3 years of completion of standard treatment. Patients' data were computed using descriptive statistics and the associations between patients' factors and the risk of early mortality were tested using the binary logistic regression model.

Results: Early deaths occurred in 36 (38.7%) of patients with EOC. In the final multivariate analyses, early tumor relapse within 6-months of treatment completion was the only independent risk factor that predicts early mortality in EOC patients (risk ratio = 8.6, 95% confidence interval: 3.3–24.5, $p < 0.01$).

Conclusion: Our study suggests that early tumor relapse may be a useful surrogate of early mortality in EOC. However, our findings should be interpreted with caution pending further corroboration through an adequately powered, prospective multicenter study.

KEYWORDS

early death, epithelial ovarian cancer, mortality, overall survival, tumor relapse

1 | INTRODUCTION

Ovarian cancer is the second most common gynecologic cancer in Nigeria[1] with the highest incidence seen among women above the age of 50 years.[2] An estimated 90% of all ovarian cancer are of epithelial origin[3] with more than 70% of these cases diagnosed at the later stages of the disease.[2] The overall 5-year survival rate of patients with epithelial ovarian cancer (EOC) is about 30%–48% despite the standard treatment of surgery and chemotherapy[4,5] with only a very modest increase of about 2%–4% since 1995.[6] Since the early 1970s, the prognosis of EOC has not improved substantially despite the substantial investments in the development of new cancer therapeutics.[7]

Several clinical and laboratory factors have been reported to influence the survival of EOC patients including age,[8] menopausal status,[9] tumor stage,[10,11] postoperative residual tumor volume,[12,13] tumor histology,[14,15] presence of ascites,[16] and pretreatment serum concentrations of cancer antigen-125 (CA-125).[17] Most of these patient-specific and tumor characteristics were also found to be strongly associated with mortality in a large study conducted recently by Peres et al.[18] involving the secondary data analysis of over 35,000 women with EOC in 2004–2016 that were extracted from the Surveillance, Epidemiology, and End Results (SEER) program. However, these strong associations were only found in the years following cancer diagnosis as the impact of these factors decreases steadily with increasing survival time.[18] A risk-stratification strategy using some of these patient and tumor characteristics is now being used to predict mortality risk and to identify EOC patients that require more intensive and individualized follow-up surveillance plans. This is even more important in resource-limited settings with a much higher early mortality rate in ovarian cancer patients as they advance through the survival trajectory.[11] This current study, therefore, focused on identifying these important risk predictors of early mortality in EOC patients managed and followed up over 10 years period at the women's cancer unit of a university teaching hospital in Southwest Nigeria.

2 | MATERIALS AND METHODS

2.1 | Study design and settings

This was a retrospective cohort study of all EOC cases who completed the standard treatment and were followed up between January 2011 and December 2020 at a university teaching hospital in Southwest Nigeria. The hospital is a foremost tertiary health institution in Southwest Nigeria that serves mainly as a specialized referral center for other government-owned and private hospitals in Lagos, Ogun, and Oyo States. The hospitals provide varieties of in-patient and out-patient multidisciplinary oncology care including gynecologic cancer.

2.2 | Eligibility criteria

We retrieved data from the medical records of women who were treated for EOC and completed up to 3-years of follow-up in the women's cancer unit from January 2011 to December 2020. The inclusion criteria were: (1) patients with EOC confirmed by histopathology; (2) patients who had a full course of standard primary treatment consisting of either primary debulking surgery (PDS) and postoperative adjuvant chemotherapy (ACT) or pre-operative neoadjuvant chemotherapy (NACT), interval debulking surgery (IDS), and postoperative adjuvant chemotherapy (ACT); (3) patients with complete medical records and laboratory test results required for data analyses. The exclusion criteria were: (1) patients who did not complete their treatment; and (2) patients with severe postoperative complications requiring intensive care admission for monitoring.

2.3 | Participants' recruitment and data collection

We included the data of 93 patients with histologically diagnosed EOC in the study. The patients' relevant data such as age, menopausal status, parity, pre-existing medical comorbidity (including diabetes mellitus, hypertension, liver, and kidney disorders), body mass index (BMI) defined as body weight in kilograms divided by the square of height in meters, laboratory findings at initial assessments (such as serum CA-125 levels and hematological parameters), International Federation of Gynecology and Obstetrics (FIGO) stage of the disease, presence of ascites and histologic subtype of the tumor were retrieved from the medical records. The final data to assess early mortality risk were collected for up to 3-years posttreatment follow-ups until December 2020. In the study, we defined standard primary treatment of EOC as a full course of treatment consisting of either PDS and six-cycles of platinum-based postoperative ACT administered intravenously every 3 weeks or IDS in-between three and four cycles each of platinum-based pre-operative NACT and postoperative ACT administered intravenously every 3 weeks; while early mortality is defined as death occurring within 3 years of completion of standard primary treatment.

2.4 | Statistical analysis

R Statistical Computing Software (R-4.1.2) for Windows was used for data analyses and we computed descriptive statistics for the patients' sociodemographic, clinical, and laboratory characteristics. Continuous variables were presented as mean and standard deviation if normally distributed or median and interquartile range if skewed while categorical variables were presented as frequencies and percentages. Risk ratios (RR) and 95% confidence interval (CI) of early mortality risks were estimated for all patients' characteristics using a predictive model in the binary logistic analysis. The mean or median values of all

numerical variables were used as the stratifying cut-off values in the multivariate model. Age and other variables with $p < 0.20$ were included in the adjusted multivariate models. Hypothesis tests using likelihood ratio were then adopted to select the most precise and best-fitting model while associations having $p < 0.05$ were reported as statistically significant.

2.5 | Ethical considerations

The approval for the study was obtained from the hospital's Ethics Committee (ADM/DCST/HREC/APP/3699) before access to the patients' medical records and subsequent data collection. We ensured strict adherence to the confidentiality of participants' information during the conduct and reporting of the study findings.

3 | RESULTS

We initially retrieved the data of 124 EOC patients who were diagnosed and managed with the standard first-line treatment in the hospital. Of these, 93 patients were included in the final data analyses based on the eligibility criteria (Figure 1).

The baseline characteristics of EOC patients included in the study are shown in Table 1. Early mortality was recorded in 38.7% of patients. We recorded the patient's mean age as 47.1 ± 13.9 years and the BMI as 23.6 ± 5.2 kg/m^2. We also recorded median serum CA-125 as 143 (49–577) U/ml, platelet: 314 (212–422) × 10^6 cells/L, hemoglobin: 10.5 (9.4–11.4) g/dL, and WBC: 6.2 (4.7–7.6) × 10^6 cells/L. The patients were predominantly multiparous ($n = 50$, 53.8%), postmenopausal ($n = 52$, 55.9%), and more than four-fifths ($n = 77$, 82.8%) had co-existing medical morbidity. The majority of the patients had PDS as their upfront treatment ($n = 57$, 61.3%), no ascites ($n = 56$, 60.2%), advanced FIGO stage of the disease ($n = 65$, 69.8%), suboptimal debulking at surgery ($n = 54$, 58.1%), and type II histologic subtype of the tumor ($n = 60$, 64.5%).

Patients with EOC were stratified into two groups based on mortality within 3-years of completion of their primary treatment and factors related to their mortality risks were compared in Table 2. Based on a predefined p value of <0.20, early mortality was found to be associated with parity ($p = 0.05$), pretreatment platelet ($p = 0.09$), hemoglobin ($p = 0.02$) and white blood cell ($p = 0.17$) levels, and early tumor relapse ($p < 0.01$). However, after adjustments for other covariates in the final multivariate analysis, the occurrence of early tumor relapse (RR = 8.6, 95%CI: 3.3–24.5, $p < 0.01$) was the only independent predictor of early mortality risk in EOC patients (Table 3).

4 | DISCUSSION

This study was focused on identifying patients with EOC who received the standard primary treatment to explore the factors related to their mortality risk within 3 years of completion of treatment. The mortality of women diagnosed with EOC has plateaued since the 1970s[5] with patients typically having an estimated 5-year survival rate of 48% after completion of the standard first-line treatment comprising of surgery and platinum-based chemotherapy.[4,5] The 3-year mortality risk recorded in the current study was 38.7% equivalent to an annual death rate of 3.4%, which is higher than the annual death rate of 2.2% reported in most studies in the developed countries.[4,5] This is however similar to the early mortality risk of EOC patients reported in previous studies conducted in the same setting[8,11] and this may be attributed to the late presentation of patients due to the all-pervading poverty, ignorance, and lack of access to clinical trials, early diagnosis, and novel treatment modalities.

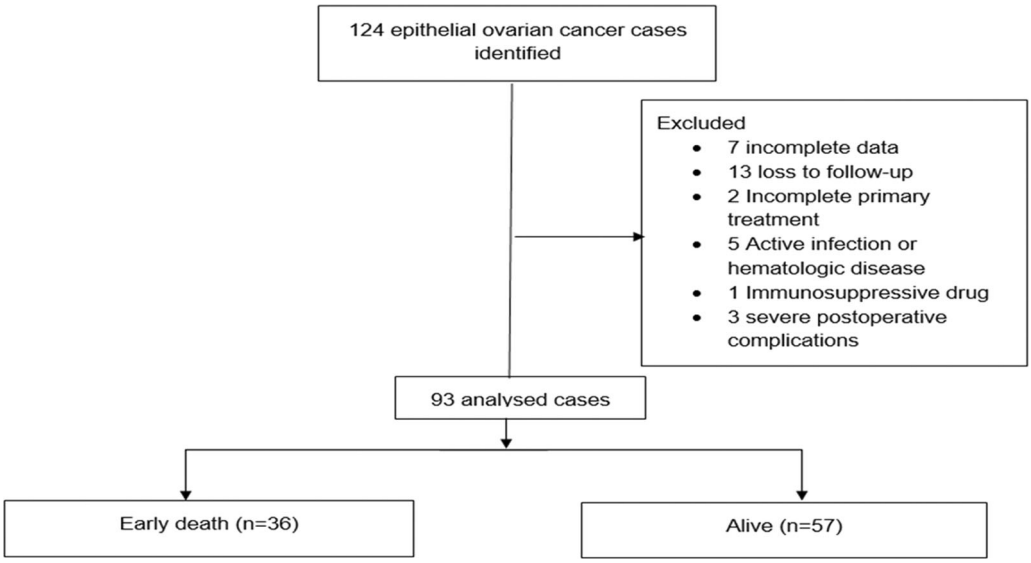

FIGURE 1 Study flow chart.

TABLE 1 Characteristics of patients with epithelial ovarian cancer ($n = 93$)

Characteristics	Number (%)
Mean age (± SD) in years	47.1 ± 13.9
Mean BMI (± SD) in kg/m^2	23.6 ± 5.2
Median serum CA-125 levels (IQR) in U/ml	143 (49–577)
Median platelet count (IQR) in cells ×10^9/L	314 (212–422)
Median hemoglobin (IQR) in g/dL	10.5 (9.4–11.4)
Median WBC count (IQR) in cells ×10^9/L	6.2 (4.7–7.6)
Parity	
Nulliparity	43 (46.2)
Multiparity	50 (53.8)
Menopausal status	
Postmenopause	52 (55.9)
Premenopause	41 (44.1)
Comorbidity	
Yes	16 (17.2)
No	77 (82.8)
Upfront treatment	
PDS	57 (61.3)
NACT	36 (38.7)
Ascites	
Yes	37 (39.8)
No	56 (60.2)
FIGO stage	
Early (I & II)	28 (30.2)
Advanced (III & IV)	65 (69.8)
Debulking status at surgery	
Optimal	39 (41.9)
Suboptimal	54 (58.1)
Histological subtype	
Type I (LGSC and others)	33 (35.5)
Type II (HGSC)	60 (64.5)
3-year mortality	
Yes	36 (38.7)
No	57 (61.3)

Abbreviations: CA, cancer antigen; FIGO, International Federation of Gynecology and Obstetrics; HGSC, high-grade serous carcinomas; IQR, interquartile range; LGSC, low-grade serous carcinomas; NACT, neoadjuvant chemotherapy; PDS, primary debulking surgery; SD, standard deviation; WBC, white blood cells.

EOC is mainly considered an age-related and postmenopausal disease[19,20] and this is evident in our study with the mean age of the patients being 47.1 years with the majority having achieved menopause (55.9%). Many studies have reported that being in the older age group is associated with a poorer outcome in EOC patients.[20–22] This is because the more advanced disease with lower overall survival rates are usually seen in women in the older age group[20,23] as these women are less likely to be treated aggressively than those in the younger age group.[24] Conversely, other studies have also stated that age is not an independent prognostic factor in EOC patients[9,25] and this was corroborated by our present study that found no association between the patients' age and mortality risk. Furthermore, pregnancy has been reported to decrease the risk of having an aggressive disease[23] with subsequent favorable mortality risk in EOC patients.[26] However, the current study failed to demonstrate the role of parity as an independent risk predictor of mortality in patients with EOC. Many recent studies have also shown that certain hematologic markers, can be used to identify individuals with a high risk of death from some tumors[27–29] including EOC.[11,30] The measurement of preoperative hematological markers is cheap, noninvasive, and relatively easy compared to using genetic molecular biomarkers.[30] Mortality was found to be associated with pretreatment platelet, hemoglobin, and white blood cell levels in our univariate analyses. However, following adjustments in the final multivariate analyses, none of these hematological markers could independently predict early mortality risk in EOC patients and these findings confirmed that these markers could be surrogates for other prognostic indicators, such as advanced-stage disease, suboptimal cytoreduction, or even medical comorbidity.[11]

The influence of early tumor relapse on the survival of EOC patients is well recognized[31] and this is corroborated by our current study where we found that early tumor relapse within 6 months of completion of treatment was the main cause of early mortality among women with EOC. An estimated 70% of the patients will have a relapse[32] with more than half of these occurring within 12 months of completion of treatment.[2] Relapsed EOC is not a curative disease and thus, strategies to reduce mortality due to EOC must focus on identifying effective measures to prevent its early relapse. This may be through prioritization of follow-up surveillance and the introduction of a more aggressive individualized treatment plan that includes the use of maintenance therapy, especially in patients with tumor relapse.

The study has a few limitations. First, this was a retrospective study that depended on effective documentation of patients' information with a high propensity for missing data. Second, the number of patients included in the study was relatively low and therefore, our findings should be interpreted with caution. Third, we adopted a 3-year follow-up in this study to minimize the impact of the high patient drop-out observed in our facility, however, this change from the standard 5-years for survival assessment could make data extrapolation more difficult. Finally, the study site is a foremost teaching hospital in Nigeria where the predominant proportion of patients with EOC present with late-stage disease, and thus the patients included in the study may not

TABLE 2 Bivariate analyses of potential predictors of 3-year mortality using the binary logistic regression model

Predictors	Death within 3 years Yes (%) N = 36	No (%) N = 57	Bivariate Risk ratio (95% CI)	p value
Age (≥48 years)	17 (47.2)	31 (54.4)	0.7 (0.3–1.9)	0.50
Parity (Multiparity)	24 (66.7)	26 (45.6)	2.4 (0.9–6.3)	0.05
Menopausal status (postmenopause)	20 (55.6)	32 (56.1)	0.9 (0.4–2.5)	0.96
BMI (≥ 24 kg/m^2)	14 (40.0)	22 (43.1)	0.9 (0.3–2.3)	0.77
Serum CA-125 (≥143 U/mL)	20 (55.6)	27 (47.4)	1.4 (0.6–3.5)	0.44
Pretreatment platelet (≥314 × 10^9 cells/L)	22 (62.9)	25 (44.6)	2.1 (0.8–5.5)	0.09
Pretreatment hemoglobin (<11.5 g/dL)	23 (65.7)	23 (40.4)	2.8 (1.1–7.5)	0.02
Pretreatment white cells count (<6.2 × 10^9cells/L)	15 (41.7)	32 (56.1)	0.6 (0.2–1.4)	0.17
Comorbidity (Yes)	6 (16.7)	10 (17.5)	0.9 (0.3–3.2)	0.91
Upfront primary treatment (PDS)	20 (55.6)	37 (64.9)	0.7 (0.3–1.7)	0.37
Ascites (Yes)	17 (47.2)	20 (35.1)	1.7 (0.7–4.2)	0.24
FIGO stage (3 & 4)	27 (75.0)	38 (66.7)	1.5 (0.5–4.4)	0.39
Surgical debulking status (Suboptimal)	22 (61.1)	32 (56.1.)	1.2 (0.5–3.2)	0.64
Histological subtype (Type II)	25 (69.4)	35 (61.4)	1.4 (0.5–3.9)	0.43
Early tumor relapse (Yes)	21 (58.3)	8 (14.0)	8.6 (2.9–26.7)	<0.01

Abbreviations: BMI, body mass index; CA, cancer antigen; CI, confidence interval; FIGO, International Federation of Gynecology and Obstetrics; PDS; primary debulking surgery; Type II includes high-grade serous carcinomas.

TABLE 3 Multivariate prediction model for 3-year mortality using the binary logistic regression model

Characteristics	Category	First model p value	Final fitting model Risk ratio (95% CI)	p value
Age	≥48 versus <48 years	0.07	–	–
Parity	Nulliparous versus multiparous	0.05	–	–
Pretreatment platelet	≥314 versus <314 × 10^9 cells/L	0.21	–	–
Pretreatment hemoglobin	<11.5 versus ≥11.5 g/dL	0.32	–	–
Pretreatment white cells count	<6.2 versus ≥6.2 × 10^9 cells/L	0.81	–	–
Early tumor relapse	Yes versus No	<0.01	8.6 (3.3–24.5)	<0.01

Abbreviation: CI, confidence interval.

be a fair representation of the general population. However, this study is the first step in generating the hypothesis for a robust and well-designed prospective study necessary for validating our findings in this study.

5 | CONCLUSION

This study revealed that early tumor relapse is an independent risk factor that can predict early mortality in patients with EOC. This suggests that early tumor relapse may be a useful surrogate of early mortality in EOC. However, our findings should be interpreted with caution pending further corroboration through an adequately powered, prospective multicenter study.

TRANSPARENCY STATEMENT

Kehinde S. Okunade affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

AUTHOR CONTRIBUTIONS

Kehinde S. Okunade: Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; software; validation; visualization; writing—original draft; writing—review & editing. **Sarah John-Olabode**: Conceptualization; data curation; funding acquisition; investigation; methodology; project administration; resources; supervision; validation; writing—review & editing. **Ephraim O. Ohazurike**: Data curation; investigation; project administration; supervision; validation; visualization; writing—review & editing. **Adaiah Soibi-Harry**: Data curation; investigation; project administration; supervision; validation; visualization; writing—original draft; writing – review & editing. **Benedetto Osunwusi**: Data curation; investigation; project administration; supervision; validation; visualization; writing—review & editing. **Rose I. Anorlu**: Conceptualization; resources; visualization; writing—review & editing.

ACKNOWLEDGEMENTS

We appreciate the invaluable assistance of the staff of the gynecologic oncology division of the hospital's medical records department of the hospital without whom access to the patients' medical records would not have been possible. We also acknowledge the immense contribution to the data retrieval and collation by resident doctors in the oncology and pathological studies unit of the department of obstetrics and gynecology. This study was conducted through the protected time support provided by the Fogarty International Center of the National Institutes of Health under Award Numbers D43TW010134, D43TW010543, and D43TW010934. The views expressed by the authors are theirs alone and do not reflect the official views of the National Institutes of Health.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Kehinde S. Okunade had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

ORCID

Kehinde S. Okunade http://orcid.org/0000-0002-0957-7389
Adaiah Soibi-Harry http://orcid.org/0000-0001-5938-3235

REFERENCES

1. Onyiaorah IV, Anunobi CC, Banjo AA, Fatima AA, Nwankwo KC. Histopathological patterns of ovarian tumours seen in Lagos University Teaching Hospital: a ten-year retrospective study. *Nig Q J Hosp Med*. 2011;21(2):114-118.
2. Okunade KS, Adetuyi IE, Adenekan M, Ohazurike E, Anorlu RI. Risk predictors of early recurrence in women with epithelial ovarian cancer in Lagos, Nigeria. *Pan Afr Med J*. 2020;36:272.
3. Kosary CL. Chapter 16: cancer of the ovary. In: Ries LAG, Young JL, Keel GE, eds. *Cancer Survival Among Adults: US SEER Program, 1988-2001*. Department of Health and Human Services; National Cancer Institute; 2007:133-144.
4. Howlader N, Noone AM, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2017, National Cancer Institute, Bethesda, MD, based on November 2019 SEER data submission, posted to the SEER website, April, 2020. https://seer.cancer.gov/csr/1975_2017/
5. Arora T, Mullangi S, Lekkala MR. Ovarian cancer. *StatPearls [Internet]*. StatPearls Publishing; 2022. https://www.ncbi.nlm.nih.gov/books/NBK567760/
6. Allemani C, Weir HK, Carreira H, et al. Global surveillance of cancer survival 1995-2009: analysis of individual data for 25,676,887 patients from 279 population-based registries in 67 countries (CONCORD-2). *Lancet*. 2015; 385(9972): 977-1010.
7. Hanai A. Trends and differentials in ovarian cancer: incidence, mortality and survival experience. *APMIS Suppl*. 1990;12:1-20.
8. Winter WE, III, Maxwell GL, Tian C, et al. Gynecologic oncology group study: prognostic factors for stage III epithelial ovarian cancer: a gynecologic oncology group study. *J Clin Oncol*. 2007;25: 3621-3627.
9. Okunade KS, Adejimi AA, Ohazurike EO, et al. Predictors of survival outcomes after primary treatment of epithelial ovarian cancer in Lagos, Nigeria. *JCO Glob Oncol*. 2021;7:89-98.
10. Karabuk E, Kose MF, Hizli D, et al. Comparison of advanced stage mucinous epithelial ovarian cancer and serous epithelial ovarian cancer with regard to chemosensitivity and survival outcome: a matched case-control study. *J Gynecol Oncol*. 2013;24(2):160-166.
11. Okunade KS, Dawodu O, Adenekan M, et al. Prognostic impact of pretreatment thrombocytosis in epithelial ovarian cancer. *Niger J Clin Pract*. 2020;23:1141-1147.
12. Bristow RE, Tomacruz RS, Armstrong DK, Trimble EL, Montz FJ. Survival effect of maximal cytoreductive surgery for advanced ovarian carcinoma during the platinum era: a meta-analysis. *J Clin Oncol*. 2002;20:1248-1259.
13. Hoskins WJ, McGuire WP, Brady MF, et al. The effect of diameter of largest residual disease on survival after primary cytoreductive surgery in patients with suboptimal residual epithelial ovarian carcinoma. *Am J Obstet Gynecol*. 1994;170:974-979.
14. Makar AP, Baekelandt M, Tropé CG, Kristensen GB. The prognostic significance of residual disease, FIGO substage, tumor histology, and grade in patients with FIGO stage III ovarian cancer. *Gynecol Oncol*. 1995;56:175-180.
15. Karimi-Zarchi M, Mortazavizadeh SM, Bashardust N, et al. The clinicopathologic characteristics and 5-year survival rate of epithelial ovarian cancer in Yazd, Iran. *Electron Physician*. 2015;7(6): 1399-1406.
16. Chi DS, Liao JB, Leon LF, et al. Identification of prognostic factors in advanced epithelial ovarian carcinoma. *Gynecol Oncol*. 2001;82: 532-537.
17. Schneider D, Halperin R, Halperin D, Bukovsky I, Hadas E. Prediction of the survival of patients with advanced ovarian cancer according to a risk model based on a scoring system. *Eur J Gynaecol Oncol*. 1998;19:547-552.
18. Peres LC, Sinha S, Townsend MK, et al. Predictors of survival trajectories among women with epithelial ovarian cancer. *Gynecol Oncol*. 2020;156(2):459-466.
19. Chornokur G, Amankwah EK, Schildkraut JM, Phelan CM. Global ovarian cancer health disparities. *Gynecol Oncol*. 2013;129(1): 258-264.
20. Chan JK, Urban R, Cheung MK, et al. Ovarian cancer in younger vs older women: a population-based analysis. *Br J Cancer*. 2006;95(10): 1314-1320.
21. Arora N, Talhouk A, McAlpine JN, Law MR, Hanley GE. Long-term mortality among women with epithelial ovarian cancer: a population-based study in British Columbia, Canada. *BMC Cancer*. 2018;18(1): 1039.

22. Chan JK, Loizzi V, Magistris A, et al. Differences in prognostic molecular markers between women over and under 45 years of age with advanced ovarian cancer. *Clin Cancer Res*. 2004;10(24):8538-8543.
23. Poole EM, Merritt MA, Jordan SJ, et al. Hormonal and reproductive risk factors for epithelial ovarian cancer by tumor aggressiveness. *Cancer Epidemiol Biomarkers Prev*. 2013;22(3):429-437.
24. Ries LA. Ovarian cancer survival and treatment differences by age. *Cancer*. 1993;71(2 Suppl):524-529.
25. Massi D, Susini T, Savino L, Boddi V, Amunni G, Colafranceschi M. Epithelial ovarian tumors in the reproductive age group: age is not an independent prognostic factor. *Cancer*. 1996;77(6):1131-1136.
26. Kim SJ, Rosen B, Fan I, et al. Epidemiologic factors that predict long-term survival following a diagnosis of epithelial ovarian cancer. *Br J Cancer*. 2017;116(7):964-971.
27. Cupp MA, Cariolou M, Tzoulaki I, Aune D, Evangelou E, Berlanga-Taylor AJ. Neutrophil to lymphocyte ratio and cancer prognosis: an umbrella review of systematic reviews and meta-analyses of observational studies. *BMC Med*. 2020;18(1):360.
28. Daher S, Lawrence YR, Dudnik E, et al. Nivolumab in non-small cell lung cancer: real world long-term survival results and blood-based efficacy biomarkers. *Front Oncol*. 2021;11:625668.
29. Chen JH, Zhai ET, Yuan YJ, et al. Systemic immune-inflammation index for predicting prognosis of colorectal cancer. *World J Gastroenterol*. 2017;23(34):6261-6272.
30. John-Olabode SO, Okunade KS, Olorunfemi G, et al. Pretreatment neutrophil-to-lymphocyte ratio: a prognostic biomarker of survival in patients with epithelial ovarian cancer. *Cureus*. 2021;13(7):e16429.
31. Chan JK, Tian C, Teoh D, et al. Survival after recurrence in early-stage high-risk epithelial ovarian cancer: a gynecologic oncology group study. *Gynecol Oncol*. 2010;116(3):307-311.
32. Amate P, Huchon C, Dessapt AL, et al. Ovarian cancer: sites of recurrence. *Int J Gynecol Cancer*. 2013;23(9):1590-1596.

How to cite this article: Okunade KS, John-Olabode S, Ohazurike EO, Soibi-Harry A, Osunwusi B, Anorlu RI. Predictors of early mortality risk in patients with epithelial ovarian cancer. *Health Sci. Rep*. 2022;5:e717. doi:10.1002/hsr2.717