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SURVIVAL STATUS AND PREDICTORS AMONG OVARIAN CANCER PATIENTS AT ONCOLOGY CENTERS, ADDIS ABABA, ETHIOPIA, 2024

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STATEMENT OF DECLARATION

I, the undersigned, a maternal and reproductive health nursing student, declare that this thesis is my original work in partial fulfilment of the requirement for the degree of Master of Science in maternal and reproductive health nursing. I have followed all ethical principles of scholarship in the preparation, data collection, data analysis, and completion of this thesis. All scholarly material that is included in the thesis has been recognized through citation. I affirm that I have cited and referenced all sources used in this document. Every effort has been made to avoid plagiarism in the preparation of this thesis..

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LISTS OF ACRONYMS AND ABBREVIATIONS

AHR	Adjusted Hazard Ratio
CHR	Crude Hazard Ratio
CA 125	Cancer Antigens 125
CI	Confidence Interval
EFMOH	Ethiopian Federal Ministry of Health
FIGO	Federation of international Gynecology and Obstetrics
GLOBOCAN	Global Burden of Cancer
HR	Hazards Ratio
LMIC	Low- and Middle income countries
OC	Ovarian Cancer
SPHMMC	St' Paul Hospital Millennium Medical College
SSA	Sub-Saharan Africa
TASH	Tikur Anbesa Specialized Hospital

TABLE OF CONTENTS

APPROVAL BY THE BOARD OF EXAMINATION ii
STATEMENT OF DECLARATION iii
ACKNOWLEDGEMENTS iv
LISTS OF ACRONYMS AND ABBREVIATIONS v
LIST OF TABLES viii
LIST OF FIGURES ix
ABSTRACT x
1. INTRODUCTION 1
1.1 Background 1
1.2 Statement of the problem 3
1.3 Significance of the study 5
2. LITERATURE REVIEW 6
2.1. Introduction 6
2.2. Survival status among ovarian cancer women 6
2.3. Predictors of ovarian cancer survival 8
2.3.1. Sociodemographic and reproductive health related predictors 8
2.3.2. Pathological, clinical, and treatment related predictors 9
2.4 Conceptual framework 12
3. OBJECTIVES 13
3.1 General Objectives 13
3.2 Specific Objectives 13
4. METHODS & MATERIALS 14
4.1 Study area and period 14
4.2 Study design 14
4.3 Population 14
4.3.1 Source population 14
4.3.2 Sample population 14
4.3.3 Study population 14
4.4 Eligible criteria 15
4.4.1 Inclusion criteria 15
4.4.2 Exclusion criteria 15
4.5 Sample Size and Sampling Procedure 15
4.5.1 Sample size determination 15
4.5.2 Sampling technique and procedure 15

4.6 Study Variables 17
4.6.1 Dependent variable 17
4.6.2 Independent Variables 17
4.7 Standard and operational definitions 18
4.8. Data Collection Tools 19
4.9. Data Collection Procedure 19
4.10 Data Quality Control 20
4.11 Data Analysis Procedure 20
4.12 Ethical Considerations 21
4.13 Dissemination of the result 21
5. RESULT 22
5.1 Socio-demographic characteristics of the study participants 22
5.2. Reproductive health characteristics of the study participants 23
5.3. Clinical and histopathological characteristics of the study participants 23
5.3.1 Chief complaint of ovarian cancer patients 25
5.4. Treatment related characteristics of the study participants 26
5.5. Survival status of ovarian cancer patients 27
5.6. Overall Survival Function of ovarian cancer patients 27
5.7. Survival function among different groups of ovarian cancer patients 29
5.8. Predictors of ovarian cancer mortality 35
5.9. Testing proportional hazard assumption 37
6. DISCUSSION 39
7. LIMITATION AND STRENGTH OF THE STUDY 44
7.1. Limitation of the study 44
7.2. Strength of the study 44
8. CONCLUSION 44
9. RECOMMENDATIONS 45
REFERENCES 46
APPENDIX 52
ANNEX 1: Information sheet English version 52
ANNEXES II: Data extraction form of English version 54
ANNEX III: Revised FIGO Staging 57
ANNEX IV: Comorbidities 58

LIST OF TABLES

Table 1: Socio-demographic characteristics of ovarian cancer patients at TASH and SPHMMC, Addis Ababa, Ethiopia, from January 1st 2019 to December 31th 2023 (n=561) 22
Table 2: Reproductive health characteristics of ovarian cancer patients at TASH and SPHMMC, Addis Ababa, Ethiopia, from January 1st 2019 to December 31th 2023 (n=561) 23
Table 3: Clinical, histopathological and treatment characteristics of ovarian cancer patients at TASH and SPHMMC, Addis Ababa, Ethiopia, from January 1st 2019 to December 31th 2023 . 24
Table 4: Chief complaint of ovarian cancer patients at TASH and SPHMMC, Addis Ababa, Ethiopia, from Jan 1st 2019 to Dec 31th 2023 (n=561)..... 25
Table 5: Treatment related characteristics of ovarian cancer patients at TASH and SPHMMC, Addis Ababa, Ethiopia, from Jan 1st 2019 to Dec 31th 2023 (n=561)..... 26
Table 6: Life table of ovarian cancer patients at TASH and SPHMMC, Addis Ababa, Ethiopia, from January 1st 2019 to December 31th 2023 (n=561) 28
Table 7: Median survival time, cumulative survival probability, significance and log rank test to different characteristics of patients during 5-year of follow-up of ovarian cancer patients at TASH and SPHMMC, Addis Ababa, Ethiopia from Jan 1st 2019 to Dec 31th 2023 (n=561). 30
Table 8: Results of the bivariable and multivariable cox regression analysis of ovarian cancer patients at oncology centers, Addis Ababa, Ethiopia, from Jan 1st 2019 to Dec 31th 2023..... 36
Table 9: Schoenfeld residuals test assessing proportional hazards assumption on cox regression analysis of ovarian cancer patients at TASH and SPHMMC, Addis Ababa, Ethiopia, from January 1st 2019 to December 31th 2023 (n=561)..... 37
Table 10: Data extraction form for the assessment of survival status and predictors among Ovarian Cancer Patients at Oncology Centers, Addis Ababa, Ethiopia, January 1st 2019-December31th 2023. 54

LIST OF FIGURES

Figure 1: Conceptual framework for the assessment of survival status and predictors among ovarian cancer patients at oncology centers, Addis Ababa, Ethiopia (36,45–47,53–64,68–74). . 12
Figure 2: Diagram presenting the sample size included in the study from January 1st 2017 to December 31th 2018 for the assessment of survival status and predictors among ovarian cancer patients at oncology centers, Addis Ababa, Ethiopia, 2024 16
***Figure* 3:** Overall five-year Kaplan-Meier estimation of survival functions of patients on ovarian cancer at TASH and SPHMMC, Addis Ababa, Ethiopia, from Jan 1st 2019 to Dec 31th 2023.... 27
Figure 4: The Kaplan-Meier survival curves compare survival time of ovarian cancer diagnosis with different categories of FIGO stage in TASH and SPHMMC, Addis Ababa, Ethiopia from January 1st 2019 to December 31th 2023..... 31
Figure 5: The Kaplan-Meier survival curves compare survival time of ovarian cancer diagnosis with different categories of substance use in TASH and SPHMMC, Addis Ababa, Ethiopia from January 1st 2019 to December 31th 2023..... 32
Figure 6: The Kaplan-Meier Hazard curves compare survival time of ovarian cancer diagnosis with different categories of family history of ovarian cancer in TASH and SPHMMC, Addis Ababa, Ethiopia from January 1st 2019 to December 31th 2023. 32
Figure 7: The Kaplan-Meier survival curves compare survival time of ovarian cancer diagnosis with different categories of contraceptive use in TASH and SPHMMC, Addis Ababa, Ethiopia from January 1st 2019 to December 31th 2023. 33
Figure 8: The Kaplan-Meier Hazard curves compare survival time of ovarian cancer diagnosis with different categories of treatment completion in TASH and SPHMMC, Addis Ababa, Ethiopia from January 1st 2019 to December 31th 2023. 33
Figure 9: The Kaplan-Meier survival curves compare survival time of ovarian cancer diagnosis with different categories of menopausal status in TASH and SPHMMC, Addis Ababa, Ethiopia from January 1st 2019 to December 31th 2023. 34
Figure 10: The Kaplan-Meier Hazard curves compare survival time of ovarian cancer diagnosis with different categories of comorbidity in TASH and SPHMMC, Addis Ababa, Ethiopia from January 1st 2019 to December 31th 2023..... 34
Figure 11: Cox-Snell residual Nelson -Aalen cumulative hazard graph on ovarian cancer patients in TASH and SPHMMC, Addis Ababa, Ethiopia, from January 1st 2019 to December 31th 2023 38

ABSTRACT

Introduction: Ovarian cancer is the leading cause of death and has the worst prognosis among gynaecologic malignancies worldwide. In Ethiopia, ovarian cancer is the third most prevalent gynaecologic malignancy, following breast and cervical cancers. One of the key aspects of the strategic framework of the Ethiopian Federal Ministry of Health is to minimize the incidence and mortality of cancer as well as improve the quality of life of cancer patients. The survival rate of ovarian cancer has improved significantly with early detection and treatment. Despite extensive studies on the subject, studies on survival rate of ovarian cancer patients are still scarce.

Objective: The main aim of this study was to assess the survival status and predictors among Ovarian Cancer Patients at Oncology Centers, Addis Ababa, Ethiopia, 2024.

Method: A facility-based retrospective cohort study was conducted in oncology centers in Addis Ababa. All cases of ovarian cancer registered from January 1st, 2017 to December 31st, 2018 in Addis Ababa oncology centers were followed retrospectively for five-year survival (until December 31st, 2023). Descriptive statistics were used, and to determine the presence of differences in survival rate among predictors, Kaplan-Meier survival curve and log rank test were performed. The net effect of each predictor variable on time to death after ovarian cancer diagnosis was estimated using Cox regression at the 5% level of significance.

Result: The study involved a total of 561 patients with ovarian cancer. Of these, 264 (47.1%) patients were died, yielding a crude mortality rate of 16.67 per 100(95%CI: 14.78–18.81) person-years. Overall, the median survival time was 43.4(95% CI, 40.39–47.37) months. The cumulative estimated 5-year survival rate following the diagnosis of ovarian cancer was 38.87% (95% CI, 34.05 to 43.68%). Independent predictors of mortality were advanced age (≥60) [AHR: 3.35, 95%CI: (1.23-9.18)], advanced FIGO stage (III&IV) [AHR: 2.29, 95%CI: (1.18-4.46)], and being a combined oral contraceptive user was protective [AHR: 0.45, 95%CI: (0.21-0.96)].

Conclusion and recommendation: Ovarian cancer patients had a lower overall survival rate when compared to those in high- and middle-income countries. Advanced FIGO stage, epithelial histology, advanced age, comorbidity, being a combined oral contraceptive user, chemo-surgery treatment mode, and treatment completion were significant predictors of mortality in ovarian cancer patients. As a result, early screening, early stage diagnosis, and early treatment should be emphasized since advanced stages are associated with high mortality.

K**eywords:** Ovarian cancer patients, Predictors, Incidence, Time to death, survival status, Death.

1. INTRODUCTION

1.1 Background

Ovarian cancer is a malignant tumor that originates in the ovaries and can spreads beyond the ovaries. The symptoms are often remain uncertain, rendering early detection difficult, hence the vast majority of patients present with advanced-stage disease(1).

Ovarian cancer is not a single disease and can be subdivided into at least five different histological subtypes that have different identifiable risk factors, cells of origin, molecular compositions, clinical features, and treatments (2). The most common type and leading cause of mortality is attributed to epithelial ovarian cancer, it begins in the cells that cover the ovary (3,4).

Ovarian cancer is a leading cause of mortality worldwide and the seventh most commonly diagnosed malignancy among all forms of cancer in women(5,6) and the third most prevalent gynecological cancer globally, following cervical and uterine cancer(7). Approximately 207, 252 new deaths from ovarian cancer were reported globally in 2020(8), account for 4.4% of all cancer-related mortality among women(9).

In Sub-Saharan Africa (SSA), ovarian cancer (OC) is the second most prevalent gynaecological cancer. Despite its rising public health threat, incidence rates remain low in Africa(10). However, due to the lack of cancer registration in most African countries, precise incidence data are not available. Based on Global Burden of Cancer (GLOBOCAN) 2018 data estimation in the SSA region, 18,000 women developed ovarian cancer case and 13,000 death due to ovarian cancer, resulting in 2.2% of all cancer cases(11,12).

According to Global Burden of Cancer 2020, ovarian cancer ranks as the third most common gynaecologic cancer, next to breast and cervix cancers, which account for 3.4% of cancer cases and 3.6% of cancer mortality among women in Ethiopia(13). Based on a report from the Addis Ababa cancer registry, Ethiopia has an age-standardized incidence rate of ovarian cancer of 8.5 per 100,000 person-years, which is approximately double that of other Sub-Saharan countries as evidenced by global data(14).

The highest mortality rate are found in Asia, but mortality rates in Europe and North America have declined in recent years, particularly among young people. Furthermore, low rates are

reported throughout Africa(15,16). However, African women have a high mortality-to-incidence ratio, indicating a lack of access to proper treatment(17).

Ovarian cancer has the worst prognosis and is the major cause of mortality from gynecologic cancers(6). Because, lack of effective screening, delayed onset of symptoms, and the fact that early stages of ovarian cancer are often asymptomatic result in its diagnosis in the advanced stages(1,9,16,18). At the time of diagnosis, nearly 75% of women had advanced disease(16). Consequently, this cancer is known as the silent killer(9).

Survival is highly dependent on stage of disease and age of the patient: Patients with early-stage disease had a five-year overall survival rate of 80-90%, compared to 25% with advanced-stage disease. The 5-year survival declined significantly with age, from 70% in the youngest (<45 years) to 20% in the oldest age group of patients (75-99 years)(16).

In order to reduce this burden, the Ethiopian Federal Ministry of Health (MOH) has started assembling a task force to combat non-communicable diseases, including cancer, with a special emphasis. One of the essential aspects of the strategic framework is to minimize the incidence and mortality of cancer while also improving the quality of life of cancer patients(19). In accordance with this approach, this study aims to investigate the survival status and predictors among ovarian cancer patients at oncology centers in Addis Ababa, Ethiopia.

1.2 Statement of the problem

Early detection and treatment have considerably improved the survival rates of patient with ovarian cancer, but regardless of the tremendous amount of study in the field, the survival rate of ovarian cancer patients is still low and prone to high mortality. This is due to a lack of feasible early-stage diagnostic tool, the majority of patients arrive with advanced disease, and the fact that disease symptoms tend to be uncertain. These are some of the key issues associated with the low survival rate for patients with ovarian cancer(1,9,16,18,20).

Globally, early detection rate of ovarian cancer is about 20%, if effective early detection is achievable; the overall survival rate can increase by up to 70%. However, for the majority of patients, late-stage detection of advanced cancer results in a 35% survival probability(20). Early detection is challenging because of the lack of apparent earliest symptoms; hence, ovarian cancer patients are often diagnosed at an advanced stage. The current treatment methods include adjuvant chemotherapy with platinum and paclitaxel regimens and debulking surgery, which have an 80% response rate for all patients, although these patients often relapse after the initial response and eventually die due to recurrence(21).

Ovarian cancer incidence and epidemiology patterns vary around the world(17)**.** The lowest incidence rates of ovarian cancer are found in North Africa (2.6 per 100,000 person-years) as compared to developed countries (13.3 per 100,000 person-years in Northern Europe). On the African continent alone, there will be 24,000 cases of ovarian cancer in 2020, and cancer incidence in Africa is anticipated to spike by 70% between 2012 and 2030, the most rapidly rising of any region in the entire globe. This problem is considered to be multifaceted and influenced primarily by variables such as lack of cancer awareness, inadequate resources, and the presence of other critical public health concerns(22,23).

In Sub-Saharan Africa including Ethiopia, ovarian cancer is the third leading cause of cancer-related mortality among women. The incidence has been increasing over the past decade, with about 2,550 diagnosed cases and 2,000 deaths each year(12,24). This due to multifactorial problems in Sub-Saharan Africa such as late cancer diagnosis and limited access to timely and standard treatment(12). Economic development, population growth, and aging also some of the factors for the increasing incidence of cancer globally(25).

Globally, patients with ovarian cancer have only a 45.6% cumulative five-year survival rate(20). There was a broader worldwide variance in survival rate of ovarian cancer in developed as well as developing countries; hence, the disparity was widest amongst older patients as well as those in advanced stages of diagnosis. The relative survival rate reduced with age at diagnosis and disease stage increase(26,27).

Ovarian cancer has the lowest incidence as compared to breast cancer, but to compare ovarian cancers 5-year survival rates with breast, endometrial, or cervical cancer, 49%, 90%, 81%, and 66%, respectively. It's worth noting that ovarian cancer is the most fatal female malignancy and has a worsening rate(21,28). By 2035, the mortality will reach over 250,000 cases per year, driven by a longer life expectancy, increase in population number, and greater risk due to economic development. As a result, the effort to enhance survival and quality of life for ovarian cancer patients is an increasing and critical worldwide priority(29).

Despite the substantial knowledge regarding ovarian cancer survival rates in the developed world, cancer survival data from countries in, Asia, Central America, and Africa are not generally available(29). There is a scarcity of data on the demographics, treatment methods, and survival outcomes findings among ovarian cancer patients in Sub-Saharan Africa. Such data is required to assess the existing state of diagnosis and care for women with certain types of malignancies, and to influence the future direction of cancer care in the country(30).

Adequate survival data offer patients an insight of the nature and course of the disease, as well as help oncologists in counselling and medical treatment. Therefore, identifying the most appropriate tools for evaluating and assessing ovarian cancer survival is fundamental(31). In addition, multiple risk factors can play a role in the development of ovarian cancer. Being aware of and controlling these risk factors could potentially help to prevent ovarian cancer. Moreover, understanding the disease's survival and fatality rates can helps to develop strategies aimed at prevention and also assess the current standard of care(32).

Despite the fact that the Ethiopian government's provides a special emphasis over the problem of non-communicable diseases especially on cancer, in order to reduce the incidence and mortality rate, data regarding to the survival status of ovarian cancer patients in Ethiopia is still limited.(12). Hence, this study aimed to assess the survival status and predictors among Ovarian Cancer Patients at Oncology Centers, Addis Ababa, Ethiopia.

1.3 Significance of the study

The rationale for investigating the survival status of ovarian cancers will be practical as well as essential for patients, clinicians, and researchers. This research will help policymakers, program administrators, and health providers to evaluate patient survival rates, evidence based decision making regarding ovarian cancer, and build mechanisms for an expanded cancer control and prevention strategy.

This study will additionally provide insight for health professionals in cancer treatment centers regarding the quality and effectiveness of the services they provide. Furthermore, understanding ovarian cancer survival outcomes speeds up starting of customized treatment, eliminates unnecessary treatments, and allows healthcare professionals and patients to make more precise decisions. This will motivate clinical practice, education, and research to furnish evidence-based care that relies on new existing information and prognosis will be estimated based on evidence and local circumstances. Finally, the findings of this work will serve as a foundation for future researches.

2. LITERATURE REVIEW

2.1. Introduction

The objective of the present review of literature is to outline what's is currently available in the existing body of knowledge about ovarian cancer survival in both developed and developing nations, to address the impact of the research findings on clinical practice, and identify gaps in the survival of ovarian cancer patients in Ethiopia. As an introduction, the literature has been assessed and compiled on sociodemographic, reproductive, pathologic, clinical, and treatment-related variables which affect ovarian cancer survival rates.

2.2. Survival status among ovarian cancer women

Overall, ovarian cancer survival rates differ substantially all over the world. Internationally, the developed nations bear a greater burden of ovarian cancer than developing nations. However, developing countries had the largest proportion of age-specific mortality among ovarian cancer patients(25). Over 70% of all cancer-related mortality occurred in low- and middle-income countries (LMICs)(33).

A study that has been done in France has shown that the overall survival was 42% at 5- years. Survival among FIGO staging at five-years was 89%, 70%, 36%, and 17% for stages I, II, III, and IV, respectively. Patients with advanced age and nonsurgical initial therapy showed a worse relative survival at all stages(31). A comparable study conducted in Turkey showed that the overall 5-year survival rate was 25.5% with a median survival time of 36 months. The overall mortality at the end of the follow-up was 47.3%. The Kaplan-Meier survival curve of patients based on their age, FIGO stage, and residual tumor tends to be associated with five-year survival., and the differences were significant at $p = 0.001$, $p = 0.004$, and $p = 0.002$, respectively. Ovarian cancer patients with advanced FIGO clinical stages had a median five-year survival time of 25 months and an overall survival rate of 13.5%(34). Furthermore, a study done in Norway showed that the overall five-year median survival time was 32 months, and the survival rate was 39%. The survival curve of patients for FIGO stage and residual tumor revealed to be associated with 5-year survival(35).

According to a study that has been conducted in Denmark, overall five-year survival was 40%. Women with localized tumors had an 83% lower excess mortality risk, whereas women with distant metastases had an 82% higher excess mortality risk. The age-standardized mortality rate

was 13.1 per 100,000 at the end of the study period(36), and almost which was parallel to that of the United States, which has survival rates of 48.6% at 5-year. The survival curve of patients for each patient's age tumor revealed to be associated with 5-year survival ($p<0.001$)(37).

Similarly, a study conducted in Iran showed that a total of 169 (13.56%) patients had died, and the survival rate over 5-years was 61%. eighty-five percent for germ cell tumours and 59% for epithelial cell tumors. The Kaplan-Meier curve showed that young patients with epithelial malignancies (less than 45 years) had significantly improved 5-year survival rates and were also significant in the log rank test(38).

A population-based study that has been conducted in seven high-income countries showed that the 3-year all-ages survival ranged from 40.1% to 60.1% in Ireland and Norway, respectively(39). On the other hand, a systematic review and meta-analysis study conducted in Asian countries revealed that the survival rates of ovarian cancer after 1, 3, and 5 years were 73.65%, 61.31%, and 59.60%, respectively(32). Furthermore, a study conducted in Dakar, Senegal, showed that the cumulative survival at five years was 13.3%(40).

A study carried out in Alexandria, Egypt, revealed that the survival rates were 96%, 84%, 68%, 54%, and 46%, respectively, at 12, 24, 36, 48, and 60 months after diagnosis. Five-year survival rates for tumors in stages I to IV were 85%, 71%, 41%, and 22%, respectively. Kaplan-Meier analysis showed that advanced age (>55) and FIGO staging (III and IV) had reduced survival compared to early age, and the difference was statistically significant ($p<0.001$), and the age-standardized mortality rate was 3.16 per 100,000(41)

Additionally, the study in Ibadan, Nigeria, showed that the longest survival length was 250 weeks; this trend became apparent in premenopausal women (younger), in contrast to the 120-week survival period in postmenopausal women (older). FIGO stage I and II patients had a mean survival time of 69 weeks, however stage III and IV patients had 39 week survival time(33).

Another study that has been done in Gezira State, Sudan, showed that the five-year overall survival rate for patients with ovarian cancer was 38% with a median survival time of 31 months, and the overall mortality rate at five years was 42%. Stage III and IV patients had a median survival time of 23 and 15 months, respectively. Kaplan-Meier analysis showed that there was a significant variation in survival rates between disease stages at diagnosis ($P<0.001$)(42).

A study conducted in Botswana revealed that the 1- and 2-year cumulative survival rate were 62.8% and 43.7%, respectively, for ovarian cancer patients(30). Likewise, a research conducted in Ethiopia revealed that the cumulative survival rate was 78%, 59%, and 33.9% at 1, 2, and 5 years after diagnosis, respectively. The median survival time was 32.5 (estimate + uncertainty) months, and at the end of the study, 39.3% of ovarian cancer patients had died(43).

2.3. Predictors of ovarian cancer survival

Researches on the survival status of patients with ovarian cancer revealed that age at diagnosis, parity, contraceptive use, HIV status, family history of ovarian cancer, histological type; residual tumor size, pre-existing comorbidity, and treatment modality determine the survival time of ovarian cancer. Survival rates of patients with ovarian cancer have varied among different countries and studies. The following is an overview of some of the literature on ovarian cancer survival time and predictors.

2.3.1. Sociodemographic and reproductive health related predictors

A study conducted in the United States indicates that patients who were younger had statistically a higher chance of survival than older patients (P=0.009)(44), and another study done in Denmark revealed that 15–49 years aged women had 46% lower the risk of mortality in comparison to women aged between 60–69 years (P<0.01)(36). A similar study in Denmark showed that ovarian cancer patients aged >64 years have a higher risk of mortality than those aged ≤64 years (HR=2.33, 95%CI, 1.69–3.21)) within 181–360 days after surgery(45).

Furthermore, a study in Norway showed that age at diagnosis >75 years old has a higher risk of mortality (HR=2.80; 95%CI, 1.61-4.86) than age <45 years(35) and this finding is parallel with a study in Taiwan (P<0.001)(21) and United States (P = 0.043)(46).

A study which has been done in China shown that patients who were divorced or separated (HR=1.21, 95%CI: 1.11-1.31), widowed (HR=1.12, 95%CI: 1.04-1.20), or unmarried (HR=1.11, 95%CI: 1.03-1.19) had a higher risk of mortality than married patients(47), and another study in Japan revealed that being married was reduced risk of mortality than unmarried woman (P<0.05)(48). Additionally, a study done in Spain showed that Living close to factories could be a risk factor for ovarian cancer death(49), and a case-control study that has been done in Japan revealed that Women having a family history of breast, uterine, or ovarian cancer in their mother or sister are more likely to develop the disease and higher mortality(P<0.001)(50).

Other studies that have been done in Japan revealed that the number of live birth (P<0.01) and pregnancies (P<0.001) were strongly associated with longer survival times. However, family history of ovarian cancer (P<0.05) was associated with decreased survival(48). A study Australia showed that a pack of cigarettes smokes per day for 20 years is related with a twofold risk of dying from ovarian cancer(P<0.01)(51). Furthermore, a study that has been done in Lagos, Nigeria, revealed that ovarian patients younger than ≤ 55 years (HR=0.40; 95%CI, 0.22-0.74) and being premenopausal (HR=2.34; 95%CI, 1.16-4.75) were independent predictors of reduced overall survival after a 2-year follow-up(52).

According to a finding from Germany, the incidence of ovarian cancer by 7% (OR=0.93) using combined oral contraceptive tablets, and this reduction is particularly significant with the first utilization at less than 25 years(53). Another case control study done in Toronto, Canada, showed that using oral contraceptive pills lowered the risk of ovarian cancer (OR=0.89), as did having a live birth (P<0.001) or an induced abortion (P<0.05). The risk also decreased when the number of live birth cases increased (P<0.001)(54).

A systematic review meta-analysis conducted in the United States, Europe, Australia, and Japan showed that women with ovarian cancer who had a higher Body Mass Index (BMI) of ⩾35 have a worse survival rate (PHR: 1.12, 95%CI: 1.01-1.25)(55). Another similar study revealed that obesity in early adulthood is related with a higher death rate among ovarian cancer patients (HR, 1.60; 95% CI: 1.10-2.34). Premorbid obesity has been related to a worse outcome in women with advanced ovarian cancer (HR, 1.45; 95% CI: 1.09–1.93)(56). Additionally, a retrospective study that has been done in Romania showed that Postmenopausal patients showed a lower oncologic prognosis than pre-menopausal women (PFS 24 vs. 72 months, P= .0001, HR = 2.32)(57).

2.3.2. Pathological, clinical, and treatment related predictors

A study that has been done in United States revealed that increased comorbidity and a lack of gynecologic oncologist visits were linked to an increase the risk of death(46), and another study conducted in Norway revealed that International Federation of Gynecology and Obstetrics (FIGO) stages were significantly associated with survival time, which were FIGO stage II (HR=4.25: 95%CI, 2.51-7.20), FIGO stage III (HR=8.03: 95%CI, 5.04-12.77), FIGO stage IV (HR=11.75: 95%CI, 6.99-19.76) as compared to FIGO stage I(35). A similar study in Egypt

revealed that Stages III and IV patients had increased risk of death (HR=2.14 (95% CI: 1.29–3.57) and 4.06 (95% CI: 2.40-6.88), respectively, than Stage I patients (41).

Several studies in developing and developed nations have also revealed that ovarian cancer patients with advanced FIGO stages have a higher incidence of death than those in earlier stages (34,43–46,52,58).

Other study that has been done in France revealed that the net survival and mortality rates varied significantly related to histological type. A ten-year survival rate showed that germ cell tumors (81%) were better than epithelial tumors (32%), sex cord-stromal tumors (40%), and tumors without biopsy (8%)(59), and it's almost parallel to the study in Virginia(60). Similarly, a study in Denmark showed that ovarian cancer patients with tumors with distant metastases had a statistically significant 82% higher risk of death, while patients with localized tumors and unknown stage had a significantly reduced risk of death, 83% and 39%, respectively (36).

According to a finding from Norway, residual tumors >1 cm at the end of primary surgery have a high risk of death (HR=1.72, 95%CI, 1.33- 2.22) in comparison to residual tumors <1 cm (35), this find parallel with a study in Denmark (HR=1.84)(45) and in Ethiopia (HR=2.23)(43). Another study in United States revealed that a mean Haemoglobin level less than 12.5mg/dl is associated with overall survival (HR=2.11, 95%CI: 1.03-4.33)(61) and a study from Turkey showed that when CA-125 levels decreased, the overall 5-year survival rates were increased (P=0.004)(34). Furthermore, a study from Italy revealed that CA-125 serum level (P=0.001), stage of disease (P=0.011), and optimal debulking surgery (P<0.0001) were reported to be major prognostic variables associated with survival(62).

A study conducted in United States revealed that chemotherapy treatment was associated with a reduction in 90-day mortality (P<0.05)(46) and another study also revealed that ovarian cancer patients with Radiation therapy were lower risk of death (HR=.84, 95%CI 0.56–1.24) in comparison to no treatment taken(63).

Research findings from American College of Obstetricians and Gynecologists showed that chemotherapy has been correlated with decreased mortality for high-risk patients (HR=0.78, 95%CI, 0.71-0.85). Chemotherapy for intermediate-risk patients (stage IA-IB grade 2) was related to an estimated 26% decrease in mortality (HR=0.74, 95%CI, 0.62-0.89)(64).

Furthermore, a study done in Australia revealed that better survival was related to frequent pre-diagnosis users of non-steroidal anti-inflammatory drug (NSAID) (HR= 0.73, 95%CI: 0.55-0.97) or post-diagnosis (H = 0.65, 95%CI: 0.45-0.94). The estimates for aspirin and non-aspirin NSAIDs were nearly the same. These variations would result in a 2.5-month increase in mean survival by five years post-diagnosis(65).

In summary, only a few studies examined ovarian cancer survival in Sub-Saharan Africa in comparison with developed countries; all of these publications reveal lower survival. Fewer yet have studied possible predictors associated with decreased survival, although these often predict an unfavourable outcome. Ovarian cancer patients advanced to the FIGO stage at diagnosis; older patients with large size residual tumors after surgery have significantly increased risk of mortality. Possible predictors related to a lower survival of ovarian cancer, such as pre-existing comorbid illness like hypertension and other medical complications, CA-125 level at diagnosis, family history of ovarian cancer, marital status, combined oral contraceptive use, tumor characteristics and treatment, and symptoms related to ovarian cancer, were not yet assessed among ovarian cancer patients in Ethiopia. Therefore, the aim of this study was to assess the survival status of ovarian cancer patients and propose concrete suggestion that could be helpful to the government, health care professionals as well as patients to manage ovarian cancer and enhance survival among Ethiopian women.

2.4 Conceptual framework

The conceptual framework described below was taken from various literatures designed for study in different countries(21,34–36,43–54,58,59,61–65). It shows the effect of independent variables such as sociodemographic-related characteristics, reproductive health-related characteristics, histopathological-related characteristics, treatment-related characteristics, clinical predictors, and co-morbid illness on the dependent variable (survival status), which was adapted from different research studies and slightly modified. This study addressed survival and predictors among ovarian cancer patients at a selected hospital oncology center in Addis Ababa.

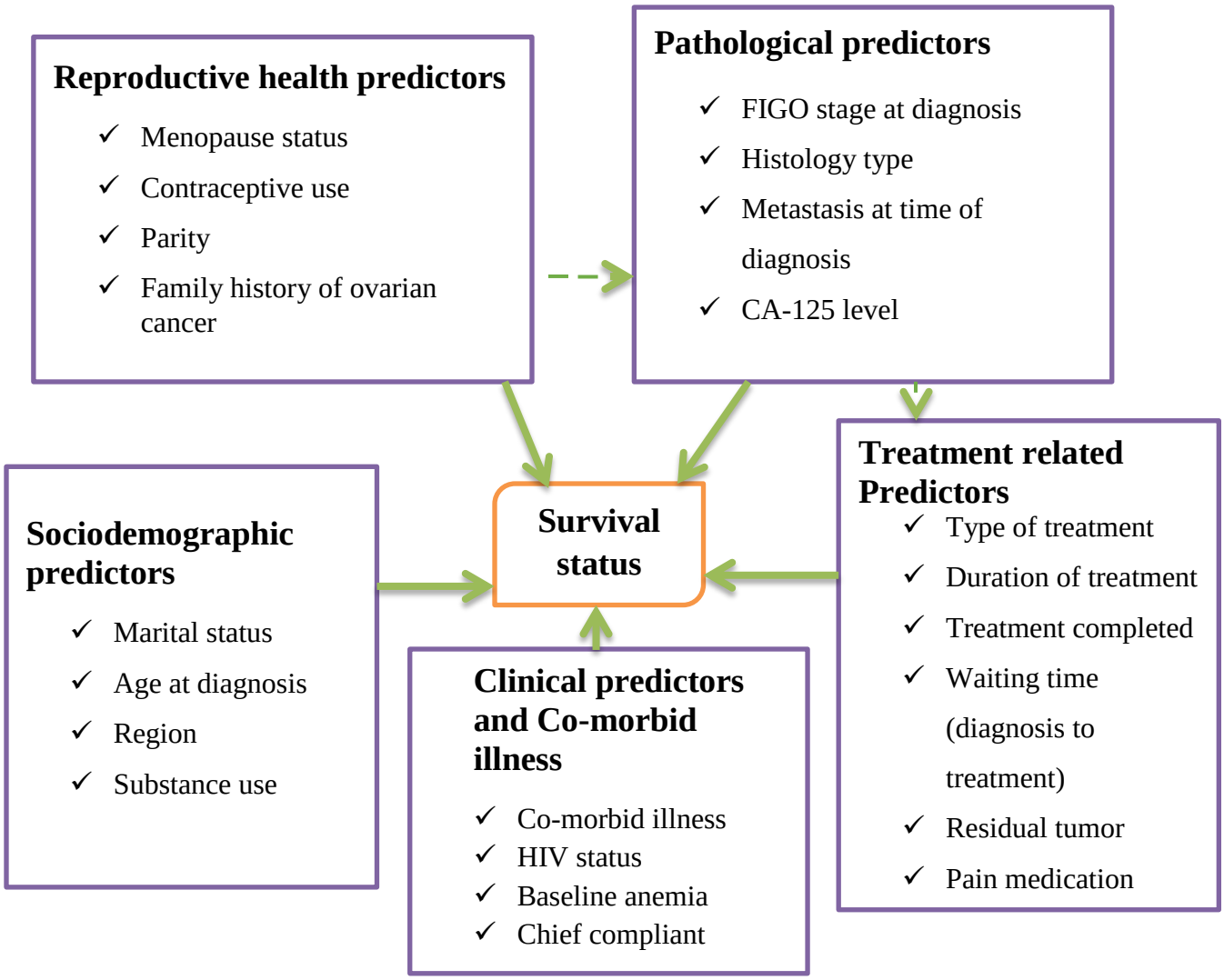

Figure 1: Conceptual framework for the assessment of survival status and predictors among ovarian cancer patients at oncology centers, Addis Ababa, Ethiopia (21,34–36,43–54,58,59,61–65).

3. OBJECTIVES

3.1 General Objectives

- To assess the survival status and predictors among ovarian cancer patients at oncology centers, Addis Ababa, Ethiopia, 2024.

3.2 Specific Objectives

- To assess the survival status of ovarian cancer patients at oncology centers, Addis Ababa, Ethiopia, 2024.
- To determine time to death of ovarian cancer patients at Oncology Centers, Addis Ababa, Ethiopia, 2024.
- To identify factors associated with ovarian cancer status of patients at Oncology Centers, Addis Ababa, Ethiopia, 2024.

4. METHODS & MATERIALS

4.1 Study area and period

The study was conducted in Addis Ababa, the capital and largest city of Ethiopia (66). The city has twelve public and more than forty private hospitals; among these, St.' Paul's Hospital Millennium Medical College (SPHMMC), and Tikur Anbessa Specialized Hospital (TASH) have their own oncology centers and given a service for more than five years, so the study was conducted among ovarian cancer patients in those two tertiary referral hospital oncology units between January 24 and February 28, 2024, in Addis Ababa, Ethiopia.

The TASH cancer center serves around 60,000 patients each year. Services are provided in both inpatient and outpatient departments. The inpatient department offers 33 patients bed capacity, while the outpatient department serves more than 850 patients per month in two clinics. Moreover, the hospital is the only cancer referral facility in the country, providing radiation therapy, chemotherapy, and surgical treatments. SPHMMC opened its oncology department in the year 2018. The center is providing all oncology services next to TASH, except for radiation treatment(67,68).

4.2 Study design

A 5-year retrospective cohort study was conducted. Patients who were newly diagnosed and enrolled in ovarian cancer treatment from January 1st, 2017 to December 31st, 2018 at SPHMMC and TASH oncology centers were followed until December 31st, 2023.

4.3 Population

4.3.1 Source population

- All women diagnosed with ovarian cancer at oncology centers in Addis Ababa.

4.3.2 Sample population

- All medical records of ovarian cancer patients who attended at oncology centers of SPHMMC and TASH between January 1st, 2017 and December 31st, 2018.

4.3.3 Study population

- All selected medical records of ovarian cancer patients who attended at oncology centers of SPHMMC and TASH between January 1st, 2017 and December 31st, 2018.

4.4 Eligible criteria

4.4.1 Inclusion criteria

All newly diagnosed ovarian cancer patients enrolled at SPHMMC and TASH during the required time (i.e., January 1st, 2017 to December 31st, 2018) were included.

4.4.2 Exclusion criteria

- Those with incomplete medical records
- Patients with absence of their medical records
- Patients who had a diagnosis at another hospital and were referred to the specified hospitals for treatment
- Clients with a history of ovarian cancer treatment

4.5 Sample Size and Sampling Procedure

4.5.1 Sample size determination

All patients with ovarian cancer who attended at the oncology centers of SPHMMC and TASH during the required time and the study were included ovarian cancer patients who met the inclusion criteria.

This time period was selected to have the nearest 5-year follow-up study time. During this time period, a total of 904 ovarian cancer patients were recorded. Hereafter, the study enrolled 561 patients who fulfilled the inclusion criteria.

4.5.2 Sampling technique and procedure

The census sampling was used, and the procedure was the following: initially, records of all ovarian cancer patients on follow-up from January 1st, 2017 to December 31th, 2018 in the SPHMMC and TASH were evaluated. Data collectors recruited study participants who fulfilled the study's inclusion criteria from a list of ovarian cancer charts who were receiving cancer care or treatment follow-up from SPHMMC and TASH oncology centers. Lastly, after exclusion based on the given criteria, the rest of the study participants were included in the study.

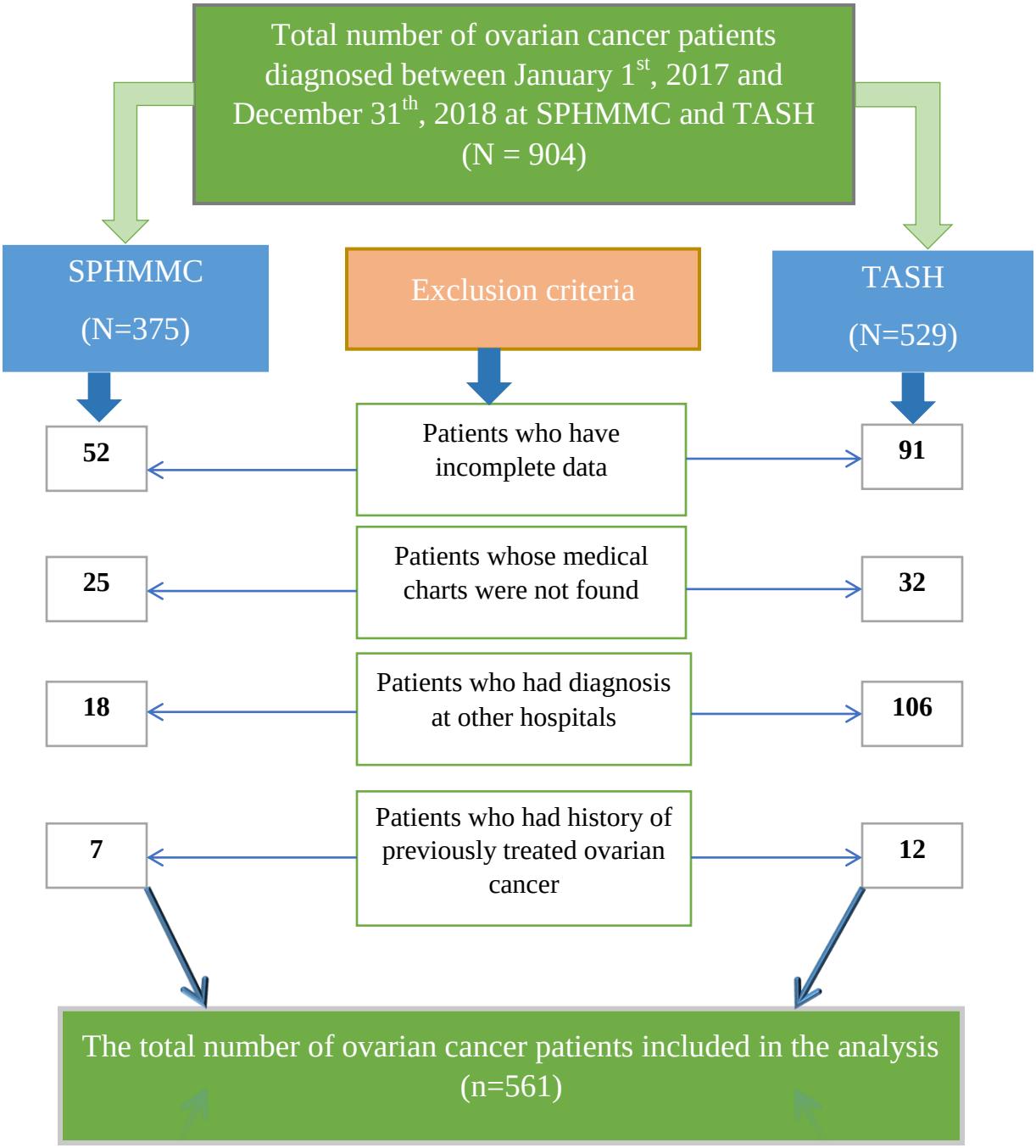

Figure 2: Diagram presenting the sample size included in the study from January 1st 2017 to December 31th 2018 for the assessment of survival status and predictors among ovarian cancer patients at oncology centers, Addis Ababa, Ethiopia, 2024

4.6 Study Variables

4.6.1 Dependent variable

- Survival status of ovarian cancer patients, which was dichotomized as 1 if ovarian cancer patients was died and 0 if censored

4.6.2 Independent Variables

- **Socio demographic predictors**
    - Marital status
    - Age at diagnosis
    - Region
    - Substance use
- **Reproductive health predictors**
    - Menopause status
    - Contraceptive use
    - Parity
    - Family history of ovarian cancer
- **Pathological Predictors**
    - FIGO stage at diagnosis
    - Histology type
    - Metastasis at time of diagnosis
    - CA-125 level
- **Treatment related Predictors**
    - Type of treatment initiated
    - Duration of treatment
    - Treatment completed/not
    - Time since diagnosis
    - Waiting time (from the date of diagnosis to treatment date)
    - Residual tumor after surgery
    - Pain medication
- **Clinical predictors and Co-morbid illness**
    - Co-morbid illness
    - HIV status
    - Baseline anemia

4.7 Standard and operational definitions

Event; The occurrence of death between the first verified date of ovarian cancer diagnosis and the completion of the study

Censored; were ovarian cancer patients who did not develop the desired outcome (death) at the end of the study period, and also those lost to follow-up, those who left against the given treatment or transferred to another health care facility throughout the study(69).

Comorbidity; Any of the conditions described in the Carlson comorbidity index, such as heart disease, liver disease, diabetes mellitus, moderate to severe CKD, and AIDS (70), other than ovarian cancer at diagnosis, which was designated a "yes", whereas the absence of these conditions at the time of diagnosis was marked as "no."

Substance use; In this study, substance usage is defined as ovarian cancer patients using one, two, or all of the two substances(cigarate and alcohol)(71).

Anemia; In this study, ovarian cancer patients with haemoglobin levels less than 12.0 g/dl were considered anemic(72).

Incomplete card: When one of the predictor variables wasn't recorded (clinical stage, histologic type, treatment type or duration, and comorbid illness status).

Index date and closing date to follow-up: The index date was the first date of definitive diagnosis of ovarian cancer, and it was used as the starting point for the survival calculation (January1st 2017 and December 31th 2018) and the closing date was December 31th, 2023.

Survival status: In this study, survival status is described as the outcome of ovarian cancer patients, and it is categorized as death or censored, which was obtained from patient medical record files from planned and unplanned visits.

Time to death: It was calculated from the date of the definitive diagnosis of ovarian cancer to the date of death, or the date censored, and estimated in months.

Stage at diagnosis: The revised International Federation of Gynecology and Obstetrics (FIGO) staging was used(73). In this study, the coding for patients diagnosed with stage IA, IB, and IC was collapsed as stage I. Stages IIA and IIB were collapsed as Stage II. Stages IIIA1, IIIA2, IIIB, and IIIC were collapsed as stage III, but stages IVA and IVB were not collapsed. All staging information reported during the first three months following the primary diagnosis was used.

4.8. Data Collection Tools

The data extraction format was derived from several literatures (21,34–36,43–54,58,59,61–65), used to collect the data and required information from the patient medical records and the registers unit in the cancer centers of TASH and SPHMMC. The data abstraction format was pretested, and the content of the included variables was examined by senior experts in the area of study (three oncologists in TASH). Data extraction was considered based on the research objectives and contains three parts: 1) a checklist related to socio-demographic and reproductive health information; 2) a checklist related to clinical, comorbidity, and histopathological predictors. 3) Checklists related to treatment predictors and survival status was obtained from the patient's medical file. Each patient's clinical stage at diagnosis was allocated using the revised International Federation of Gynaecology and Obstetrics (FIGO) staging. The survival analysis was based on the time since death, which was measured in months.

4.9. Data Collection Procedure

All the information in patients' medical files was examined, and formats from various literatures were analyzed. The proper data abstraction format in English was used to extract all relevant variables from the patient's medical file in order to achieve the study objectives. The retrospective follow-up period began at the date of the definitive diagnosis of ovarian cancer, and the endpoint was the date of death, or loss of follow-up, or against to medical treatment, or the date of transfer to another hospital, or the date of last contact until December 31th, 2023.

All medical files of ovarian cancer patients diagnosed between January 1st, 2017 and December 31th, 2018 at TASH and SPHMMC oncology units were reviewed from cancer registries. All research participants' records were selected based on the eligibility criteria. The survival status was obtained from the patient medical files or by direct call. The overall survival time was estimated as the time from the diagnosis of ovarian cancer to the date of death, or the study's end date. The records, including baseline and follow-up information, were reviewed prior to data collection, and the medical registration number was used to identify the death certificate with registration. The charts were subsequently taken out and reviewed by data collectors (4 nurses from the cancer treatment center). If all independent variables were registered but death certificates were not attached to the chart, data collectors would have made a call to the patient or patients' family or relatives using a recorded contact address on the patient chart.

4.10 Data Quality Control

The data quality was ensured by developing appropriate data extraction tools. The adopted and developed checklist content validity was examined by senior experts. A pre-test was employed on 5% (12 ovarian cancer patient charts at SPHMMC and TASH) of the sample size 15 days before the actual data collection time to examine usually documented factors in the patient's medical files and to confirm that the data extraction format matches the needs of the study. Some corrections and modifications were made to the final version of the data extraction format, i.e., remove two sociodemographic variables, "occupation" and "residency" of the patient," because almost all checked patient cards had no specific types of occupation and residency records, and add some variables like "chief compliant of the patient," "waiting time from diagnosis to treatment," and "combined oral contraceptive use".

Four nurses, who work in cancer treatment centers, collected the data. Data collectors and supervisors received one-day training in record review prior to the actual data collection task of reviewing existing records, including half-day practical and theoretical training. Data quality was maintained by developing appropriate data collection materials and providing on-going supervision. The daily inspection of data for completeness confronted problems during data collection and was addressed accordingly. Throughout data management, storage, cleaning, and analysis, all completed collection forms were reviewed for completeness and consistency. The principal investigator additionally analyzed data consistency by selecting cards at random, conducted double-data management and cleansing before analysis, and also controlled overall research activity.

4.11 Data Analysis Procedure

Data were coded and then cleaned, edited, and analyzed using STATA 17 statistical software (74). Data exploration was performed to determine whether there are any unusual codes or items that are not logical. Descriptive statistics were used to characterize the demographics, clinical, and follow-up data using frequency distribution for categorical data and central tendency and dispersion values for continuous data. The incidence density rate (IDR) was computed for the whole study period. Subsequently, the number of deaths during the follow-up was divided by the total person time at risk during the follow-up and calculated per 100 women-years. A Kaplan-Meier survival curve and a log rank test were employed to assess the changes in survival among

covariate categories, and a life table was also generated for the study subject. Prior to conducting the Cox regression model, the assumptions of proportional hazards and multi-collinearity were verified. Finally, each subject was assigned one of two outcomes: censorship or death.

A bivariable Cox-proportional hazard regression model was fitted for each explanatory variable, with a P-value ≤0.2 levels of significance in the bivariable regression were included in the multivariable analysis, a P-value of <0.05 was deemed statistically significant. The Cox-proportional hazard model assumption was checked using the Schoenfeld residual test and variables with a P-value >0.1 were considered to fulfil the assumption. Residuals were checked using the goodness-of-fit test by Cox Snell residuals, which satisfied the model test. The results of these models were expressed as hazard ratios with a 95% confidence interval and P-value. Lastly, the results of the study were presented in text, graph, and table.

4.12 Ethical Considerations

Ethical clearance and papers of approval were obtained from Addis Ababa University, College of Health Science (CHS), School of Nursing and Midwifery, Department of Midwifery Institutional Review Board (IRB),and also from Addis Ababa Health Bureau IRB and SPHMMC IRB. The school of nursing and midwifery wrote an official letter of cooperation to SPHMMC and TASH oncology centers. Then consent was obtained from the oncology centers. As the study was conducted through a review of patients' medical files, study subjects did not suffer any harm as well as confidentiality was kept. To maintain confidentiality, all collected data was coded and inaccessible by password in the computer; names and card numbers were not included in the data collection format, and the data was not shared to anyone other than the principal investigator.

4.13 Dissemination of the result

The study's findings will be submitted and presented to Addis Ababa University, CHS, School of Nursing and Midwifery, Department of Midwifery, as a partial fulfilment of masters in maternity and reproductive health nursing. It will be disseminated to other concerned bodies after approval to AAU library and to the studied health institutions (TASH and SPHMMC). The findings will also be presented in seminars, workshops, conferences, and meetings held locally or internationally, as well as published in reputable journals at the international or national level.

5. RESULT

5.1 Socio-demographic characteristics of the study participants

Between January 1st, 2017 and December 31th, 2018, 904 ovarian cancer patients were enrolled at Tikur Anbesa Specialized Hospital (529) and St' Paul Hospital Millennium Medical College (375), of which 561 were qualified for our study. The medical charts of five hundred sixty-one (264 deaths and 297 censored) ovarian cancer patients were involved in this study. The mean age of ovarian cancer patients at the time of diagnosis was 49.26 years, and SD ± 16.83 years. Nearly half, 275(49.1%) of the age group was greater than 50 years old. Approximately three-fourths, 404(72.0%) of patients were married; more than one-third, 200(35.7%) were from Addis Ababa (Table 1).

Table 1: Socio-demographic characteristics of ovarian cancer patients at TASH and SPHMMC, Addis Ababa, Ethiopia, from January 1st 2019 to December 31th 2023 (n=561)

Covariates	**Category**	**Vital status at last contact**		**Chi2 (χ^2)**	**P-value**
		Censored No. (%)	**Death No. (%)**		
Age in years at time of diagnosis	<30	83(89.2%)	10(10.8%)	138.10	<0.001
	30-39	48(72.7%)	18(27.3%)		
	40-49	80(63.0%)	47(37.0%)		
	50-59	49(52.1%)	45(47.9%)		
	≥60	37(20.4%)	144(79.6%)		
Marital status	Married	191(47.3%)	213(52.7%)	40.23	<0.001
	Single	104(73.8%)	37(26.2%)		
	Unknown	2(12.5%)	14(87.5%)		
Region	Addis Ababa	119(59.5%)	81(40.5%)	14.46	0.002
	Oromia	98(51.0%)	94(49.0%)		
	Amhara	43(39.1%)	60.9(11.9%)		
	Other*	37(62.7%)	22(37.3%)		
Substance use	User	22(32.8%)	45(67.2%)	28.06	<0.001
	Non user	170(63.9%)	96(36.1%)		
	Unknown	105(46.1%)	123(53.9%)		

* indicates regions such as, Tigray, Somali, Diredewa, Gambela, Harari, South nations nationalities and peoples (SNNP)

5.2. Reproductive health characteristics of the study participants

More than half, 344(61.3%) of the participants were postmenopausal women. Less than one-tenth, 42(7.5%) of women were combined oral contraceptive (COC) users. The reproductive health characteristics of the study participants are shown below (Table 2).

Table 2: Reproductive health characteristics of ovarian cancer patients at TASH and SPHMMC, Addis Ababa, Ethiopia, from January 1st 2019 to December 31th 2023 (n=561)

Covariates	Category	Vital status at last contact		Chi2 (χ^2)	P-value
		Censored No. (%)	Death No. (%)		
Menopause status	Premenopausal	165(76.0%)	52(24.0%)	75.77	<0.001
	Postmenopausal	132(38.4%)	212(61.6%)		
Combined oral contraceptive (COC) use	User	34(81.0%)	8(19.0%)	67.75	<0.001
	Non user	195(64.1%)	109(35.9%)		
	Unknown	68(31.6%)	147(68.4%)		
Number of parity	0-1	116(67.8%)	55(32.2%)	26.26	<0.001
	2-3	71(53.8%)	61(46.2%)		
	≥4+	110(42.6%)	148(57.4%)		
Family History of ovarian cancer	Yes	32(65.3%)	17(34.7%)	72.55	<0.001
	No	118(80.8%)	28(19.2%)		
	Unknown	147(40.2%)	219(59.8%)		

5.3. Clinical and histopathological characteristics of the study participants

More than one-third, 222(39.6%) of the participants had clinical stage III ovarian cancer at the time of diagnosis. Epithelial type was the predominant, 331(80.5%) histology type of ovarian cancer. More than half, 381(67.9%) of women had cancer metastasis at the time of diagnosis. The majority, 501(89.3%) of participants tumor markers (CA 125) were elevated. Slightly less than one-third, 153(27.3%) of women had co-morbid pre-existing medical problems. Majority, 486(86.6%) of participants were HIV-negative. Slightly more than half, 330(58.8%) of the women were anemic. The clinical and histopathological characteristics of the study participants are shown below (Table 3).

Table 3: Clinical, and histopathological characteristics of ovarian cancer patients at TASH and SPHMMC, Addis Ababa, Ethiopia, from January 1st 2019 to December 31th 2023 (n=561)

Covariates	Category	Vital status at last contact		Chi2 (χ^2)	P-value
		Censored No. (%)	Death No. (%)		
FIGO Stage at diagnosis	Stage I	53(82.8%)	11(17.2%)	117.38	<0.001
	Stage II	96(79.3%)	25(20.7%)		
	Stage III	111(50.0%)	111(50.0%)		
	Stage IV A	31(33.3%)	62(66.7%)		
	Stage IV B	6(9.8%)	55(90.2%)		
Histology type	Epithelial	210(45.0%)	257(55.0%)	71.78	<0.001
	Germ cell	39(88.6%)	5(11.4%)		
	Sex cord-stromal	38(97.4%)	1(2.6%)		
	Others*	10(90.9%)	1(9.1%)		
Metastasis at time of diagnosis	Yes	153(40.2%)	228(59.8%)	77.89	<0.001
	No	144(80.0%)	36(20.0%)		
CA-125 elevated (>35MIU/ml)	Yes	237(47.3%)	264(52.7%)	59.72	<0.001
	No	59(98.2%)	1(1.8%)		
Co-morbid illness	Yes	49(32.0%)	104(68.0%)	36.94	<0.001
	No	248(60.8%)	160(39.2%)		
HIV status	Positive	20(46.5%)	23(53.5%)	3.03	0.219
	Negative	264(54.3%)	222(45.7%)		
	Unknown	13(40.6%)	19(59.4%)		
Baseline anemia	Yes	110(47.6%)	121(52.4%)	4.47	0.035
	No	187(56.7%)	143(43.3)		

* Indicates other histologic types such as Borderline, Leiomyosarcoma, Choriosarcoma, Mixed, Fibrosarcoma, Cytology only/no pathology.

5.3.1 Chief complaint of ovarian cancer patients

Slightly more than half, 323(57.6%) of the women had a chief complaint of preoperative ascites. About one-third, 155(27.6%) of the participants had constipation. Slightly more than one tenth, 95(16.9%) of the women had a complaint of shortness of breath. Majority, 486(86.6%), and 447(79.7%) of the participants had abdominal pain and weight loss at the time of diagnosis, respectively (Table 4).

Table 4: Chief complaint of ovarian cancer patients at TASH and SPHMMC, Addis Ababa, Ethiopia, from Jan 1st 2019 to Dec 31th 2023 (n=561)

Chief complaints	Category	Vital status at last contact		Total No. (%)
		Censored No. (%)	Death No. (%)	
Abdominal distension/mass	Yes	280(51.9%)	259(48.1%)	539(96.1%)
	No	17(77.3%)	5(22.7%)	22(3.9%)
Abdominal pain	Yes	228(46.9%)	258(53.1%)	486(86.6%)
	No	69(92.0%)	6(8.0%)	75(13.4%)
Vaginal bleeding	Yes	27(52.9%)	24(47.1%)	51(9.1%)
	No	270(52.9%)	240(47.1%)	510(90.9%)
Weight loss	Yes	199(44.5%)	248(55.5%)	447(79.7%)
	No	98(86.0%)	16(14.0%)	144(20.3%)
Preoperative ascites	Yes	89(27.6%)	234(72.4%)	323(57.6%)
	No	208(87.4%)	30(12.6%)	238(42.4%)
Loss of appetite	Yes	199(47.5%)	220(52.5%)	419(74.7%)
	No	98(69.0%)	44(31.0%)	142(25.3%)
Constipation	Yes	52(33.5%)	103(66.5%)	155(27.6%)
	No	245(60.3%)	161(39.7)	406(72.4%)
Vomiting	Yes	24(24.2%)	75(75.8%)	99(17.6%)
	No	273(59.1%)	189(40.9%)	462(82.4%)
Fatigue	Yes	29(29.9%)	68(70.1%)	97(17.3%)
	No	268(57.8%)	196(42.2%)	464(82.7%)
Shortness of breath	Yes	2(2.1%)	93(97.9%)	95(16.9%)
	No	295(63.3%)	171(36.7%)	466(83.1%)
Others*	Yes	23(18.0%)	105(82.0%)	128(22.8%)

* Indicates other chief compliant of the patient such as cough, leg swelling, insomnia, frequency & urgency of urination, night sweeting, anorexia, backache and bloating

5.4. Treatment related characteristics of the study participants

Chemotherapy and surgery were the predominant, 401(71.5%) modes of treatment. Slightly more than half, 294(52.4%) of the participants took the treatment for <19 weeks of duration. Nearly more than one-third, 204(36.4%) of the women completed their treatment. Nearly half, 276(49.2%) of the women were waiting more than 19 weeks to get treatment since diagnosis. More than half, 340(60.6%) of the study participants had residual tumors after surgery. Less than half, 241(43.0%) of the women received pain medication. The treatment related characteristics of the study participants are shown below (Table 5).

Table 5: Treatment related characteristics of ovarian cancer patients at TASH and SPHMMC, Addis Ababa, Ethiopia, from Jan 1st 2019 to Dec 31th 2023 (n=561)

Covariates	Category	Vital status at last contact		Chi2 (χ^2)	P-value
		Censored No. (%)	Death No. (%)		
Type of treatment	Chemotherapy and surgery	175(43.6%)	226(56.4%)	21.91	<0.001
	Surgery	115(94.3%)	7(5.7%)		
	Chemotherapy	6(30.0%)	14(70.0%)		
	Palliative care	1(14.3%)	6(85.7%)		
	Others *	1(9.1%)	10(90.9%)		
Duration of treatment	<19week	175(59.5%)	119(40.5%)	10.74	0.001
	≥19week	122(45.7%)	145(54.3%)		
Treatment completed	Yes	147(72.1%)	57(27.9%)	47.03	<0.001
	No	150(42.0%)	207(58.0%)		
Waiting time (diagnosis to treatment)	≤10weeks	194(60.8%)	125(39.2%)	18.40	0.001
	>10weeks	103(42.6%)	139(57.4%)		
Residual tumor after surgery	Yes	138(40.6%)	202(59.4%)	111.93	<0.001
	No	121(95.3%)	6(4.7%)		
	Unknown	32(53.3%)	28(46.7%)		
Pain medication received	Yes	87(36.1%)	154(63.9%)	48.10	<0.001
	No	210(65.6%)	110(34.4%)		

* Indicates other types of treatment Chemo-Radiotherapy, Chemo-Radiotherapy + Surgery, Surgery + Radiotherapy,

5.5. Survival status of ovarian cancer patients

The cohort's overall five year mortality rate throughout the 1,584 person-years of observation (PYO) was 16.67 per 100 (95% CI: 14.78-18.81) person-years of follow-up. In this study, the overall incidence of patients who died over the course of five years was 264 (47.1%), with a confidence interval (95% CI, 42.9-51.2%). However, 297(52.9%) were censored until the end of the study. Of these, 128(22.82%) were alive, 84(14.97%) were lost to follow-up, 56(9.98%) were against medical advice, and 29(5.17%) were transferred to another institution.

5.6. Overall Survival Function of ovarian cancer patients

In our study, 561 ovarian cancer patients were followed for a total of 60 months and the median survival time was 43.4(95% CI, 40.39–47.37) months. According to Kaplan-Meier survival estimation, the overall calculated survival rate following diagnosis of ovarian cancer was 38.87% (95% CI, 34.05 to 43.68%) at 60 months of follow-up (Figure 3).

The estimated overall survival rate was 95.3%, 78.4%, 57.7%, 44.7%, and 38.9% at 12, 24, 36, 48, and 60 months, respectively (Table 6). The Kaplan-Meier survival curve shows when the follow-up time increases likelihood of survival was decreased, which is a common feature of survival data analyses. As seen on the Kaplan-Meier survival curve, the most significant rate of mortality occurred between the follow-up time of 20 and 40 months after OC diagnosis.

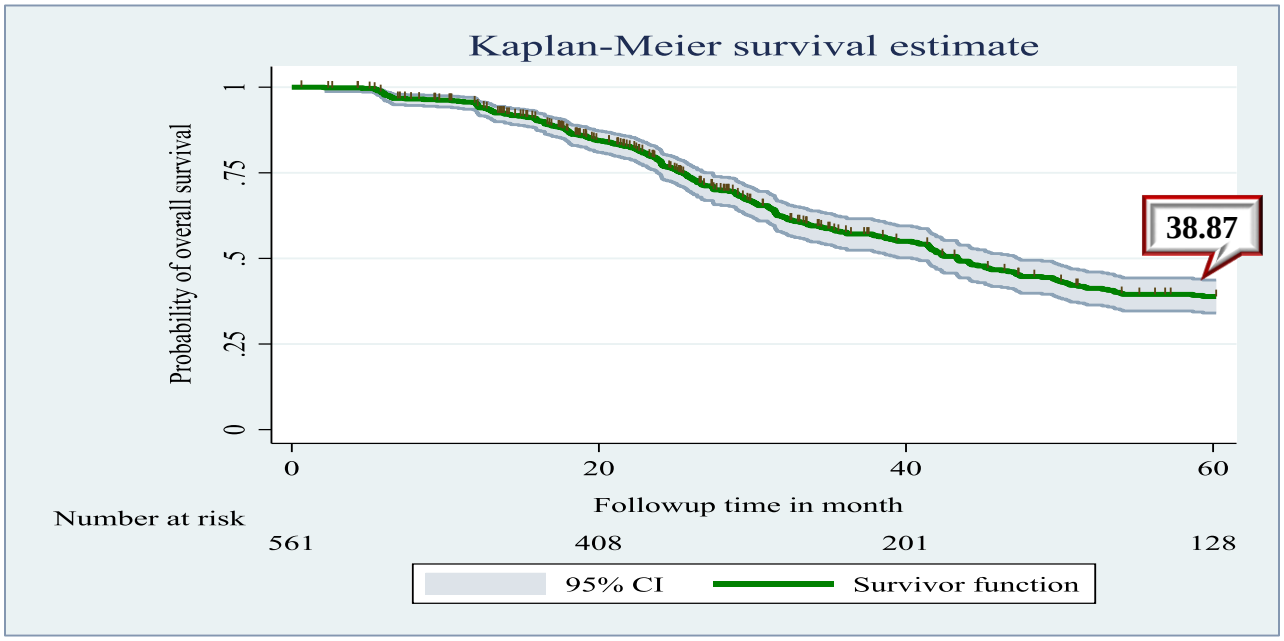

Figure 3: Overall five-year Kaplan-Meier estimation of survival functions of patients on ovarian cancer at TASH and SPHMMC, Addis Ababa, Ethiopia, from Jan 1st 2019 to Dec 31th 2023.

Table 6: Life table of ovarian cancer patients at TASH and SPHMMC, Addis Ababa, Ethiopia, from January 1st 2019 to December 31th 2023 (n=561)

Interval Start Time (Month)	Number Entering Interval	Number of Withdrawing during Interval	Number Exposed to Risk	Number of Terminal Events	Proportion Surviving	Cumulative Proportion Surviving at End of Interval	Hazard Rate
0	561	21	550.50	26	0.95	0.95	0.00
12	514	74	477.00	84	0.82	0.78	0.02
24	356	50	331.00	87	0.74	0.58	0.03
36	219	15	211.50	47	0.78	0.45	0.02
48	157	9	152.50	20	0.87	0.39	0.01
60	128	128	64.00	0	1.00	0.39	0.00

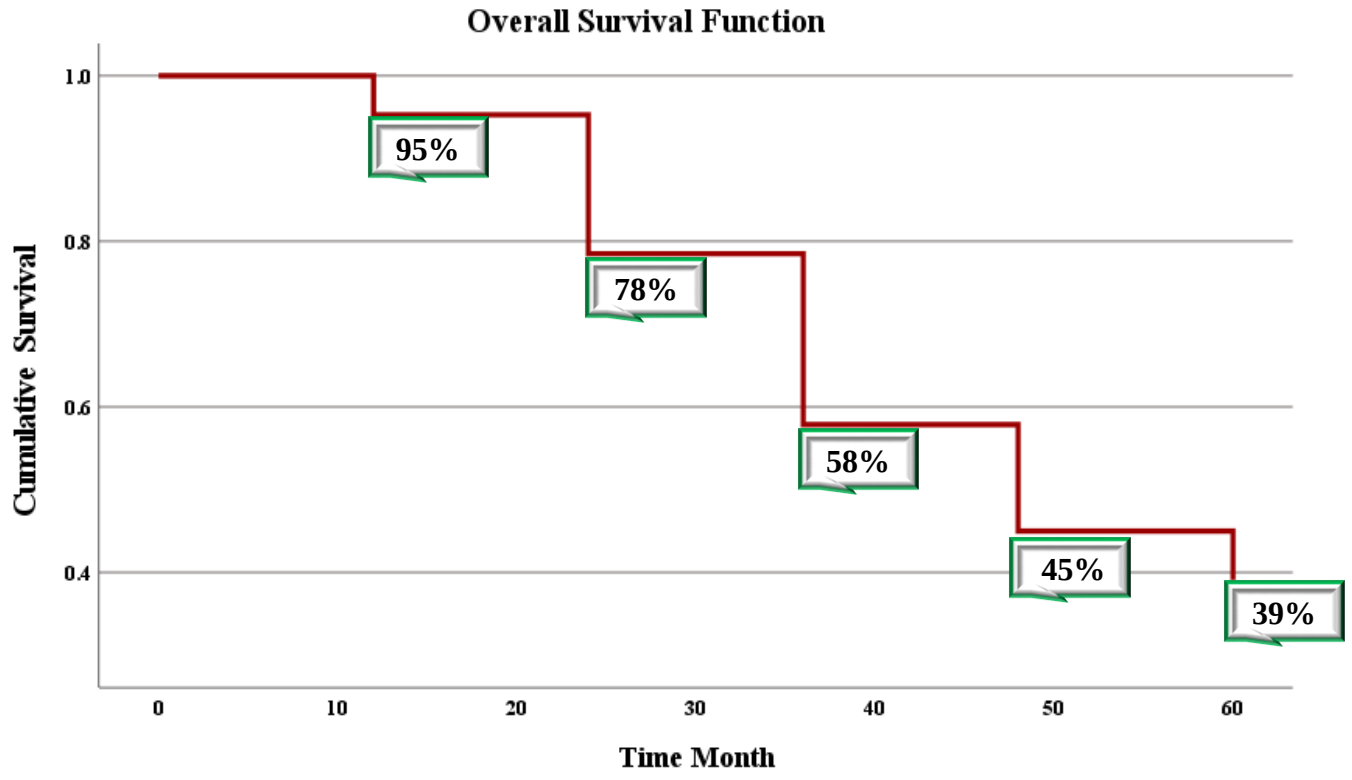

Figure 3: Survival function of ovarian cancer patients by year at TASH and SPHMMC, Addis Ababa, Ethiopia, from January 1st 2019 to December 31th 2023 (n=561)

5.7. Survival function among different groups of ovarian cancer patients

In the present study, the equality of survival curves and the presence of any significant differences in survival time among different categorical variables were tested using log-rank test. The test statistics showed that there is a significant difference in survival function for different categories of FIGO stage at diagnosis, marital status, substance use, menopausal status, contraceptive (COC) use, number of parity, family history of ovarian cancer, pre-existing co-morbid illness, metastasis at time of diagnosis, residual tumor after surgery, and treatment completion at p-value <0.05.

A significant evidence of disparity in survival time between different levels of categorical variables was seen in the Kaplan-Meier analysis. This study revealed that those who were married had a longer median survival time as compared to those whose marital status was unknown (39.44 months, 95%CI: 34.26-44.63). The difference was statistically significant (p-value < 0.001). The median survival time for substance user women was shorter than that of non-users (22.60 months, 95% CI: 16.43-28.77). This difference was statistically significant (p-value < 0.001). Women's who had clinical stage I or II at baseline had a longer median survival time than those in advanced clinical stage III and IV (32.27 months, 95%CI: 30.09-35.72), this difference was statistically significant (p-value < 0.001).

The cumulative 5-year survival for those who use combined oral contraceptives had a higher survival rate (71.06%, 95%CI: 49.81-84.58) than for those who do not use combined oral contraceptives (47.03%, 95%CI: 39.68-54.02). This difference was statistically significant (p-value < 0.001). The overall 5-year survival for those who had no pre-existing co-morbid illness had a higher survival rate (47.27%, 95%CI: 41.30-53.00) than for those who had pre-existing co-morbid illness (20.59%, 95%CI: 13.86-28.26), this difference was statistically significant (p-value < 0.001). The overall 5-year survival for those who had no family history of ovarian cancer had a higher survival rate (71.99%, 95%CI: 61.58-80.03) than for those who had family history of ovarian cancer (47.15%, 95%CI: 27.60-64.46), this difference was statistically significant (p-value < 0.001). (See table 6 and figures 4, 5, 6, 7, 8, 9, 10, 11, and12).

Table 7: Median survival time, cumulative survival probability, significance and log rank test to different characteristics of patients during 5-year of follow-up of ovarian cancer patients at TASH and SPHMMC, Addis Ababa, Ethiopia from Jan 1st 2019 to Dec 31th 2023 (n=561).

Covariates	Category	Median survival time, In month (95% CI)	Overall 5-year Survival (%)	Log rank test (χ^2)	P-value
Marital status	Married	39.44(34.26-44.63)	32.91	38.34	<0.001
	Single	**	61.77		
	Unknown	22.40(14.47-30.33)	12.50		
Substance use	User	22.60(16.43-28.77)	10.79	79.00	<0.001
	Non user	**	51.21		
	Unknown	33.82(28.04-39.59)	32.38		
Menopausal status	Premenopausal	**	64.60	64.68	<0.001
	Postmenopausal	32.34(29.70-34.97)	24.95		
Contraceptive (COC) use	User	**	71.06	47.62	<0.001
	Non user	51.78(46.22-**)	47.03		
	Unknown	31.02(28.57-33.47)	24.92		
Number of parity	0-1	**	54.47	17.25	<0.001
	2-3	41.45(33.01-49.89)	36.17		
	≥4+	36.15(30.01-42.29)	31.16		
Family History of ovarian cancer	Yes	53.95(46.22-**)	47.15	50.03	<0.001
	No	**	71.99		
	Unknown	33.62(29.32-37.91)	27.32		
FIGO Stage at diagnosis	Stage I	**	80.34	293.67	<0.001
	Stage II	**	71.29		
	Advanced (Stage III & IV)	32.27(30.09-35.72)	17.22		
Co-morbid illness	Yes	38.22(30.62-45.82)	20.59	23.14	<0.001
	No	49.80(43.32-**)	47.27		
Metastasis at diagnosis	Yes	32.57(29.91-35.22)	18.64	100.85	<0.001
	No	**	74.29		
Residual tumor after surgery	Yes	35.33(30.37-40.29)	21.48	197.0	<0.001
	No	**	93.62		
	Unknown	43.36(30.54-56.17)	28.14		
Treatment completed	Yes	**	69.06	145.0	<0.001
	No	30.44(28.88-31.91)	7.8		

**values that hadn't median survival or upper confidence interval from the specific categorical variable in this research.

The Kaplan-Meier graph shows that women's who had clinical stage I or II at baseline had a longer median survival time than those in advanced clinical stage III and IV (32.27 months, 95%CI: 30.09-35.72), this difference was statistically significant (p-value < 0.001) (Figure 4).

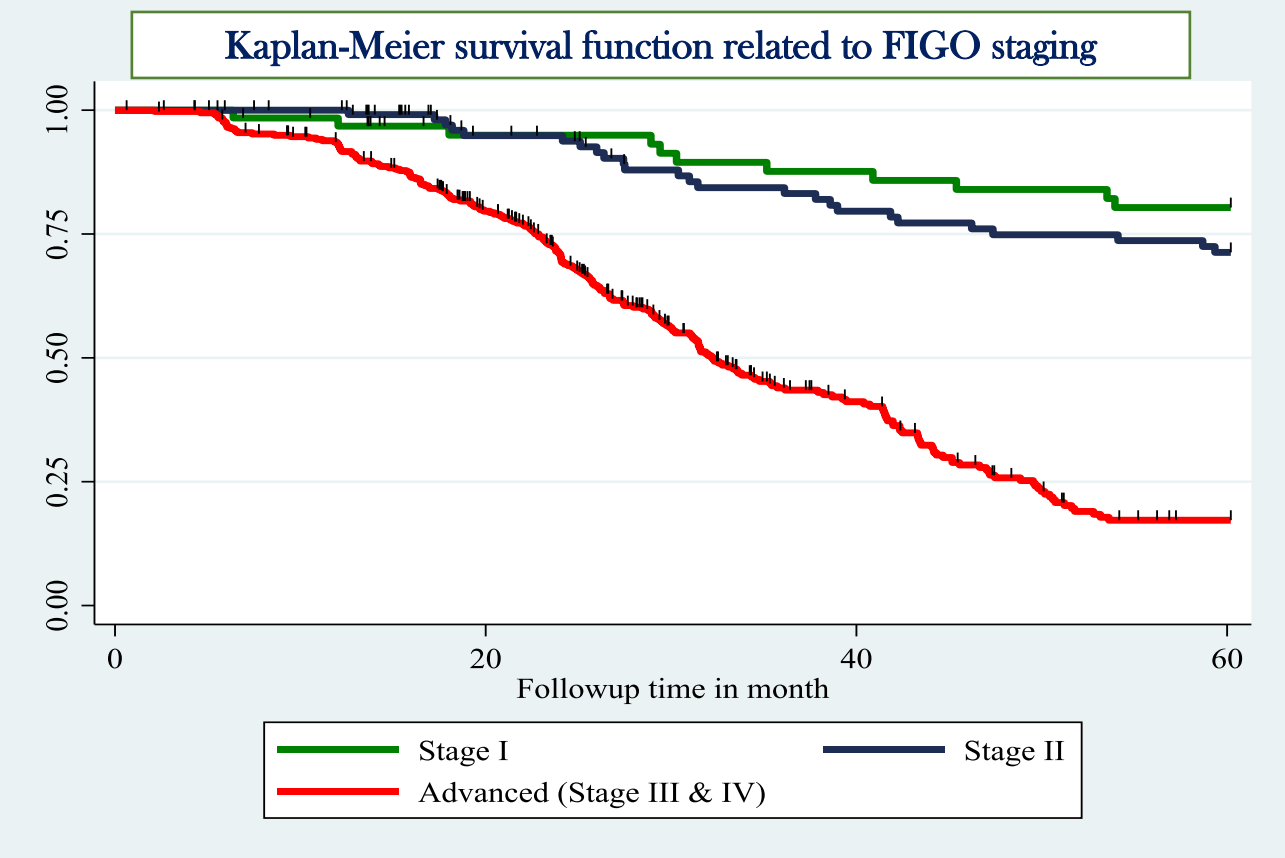

Figure 4: The Kaplan-Meier survival curves compare survival time of ovarian cancer diagnosis with different categories of FIGO stage in TASH and SPHMMC, Addis Ababa, Ethiopia from January 1st 2019 to December 31th 2023.

The Kaplan-Meier graph shows that substance user women had a shorter median survival time (22.60months, 95%CI: 16.43-28.77) than non-users. This difference was statistically significant (p-value < 0.001) (Figure 5).

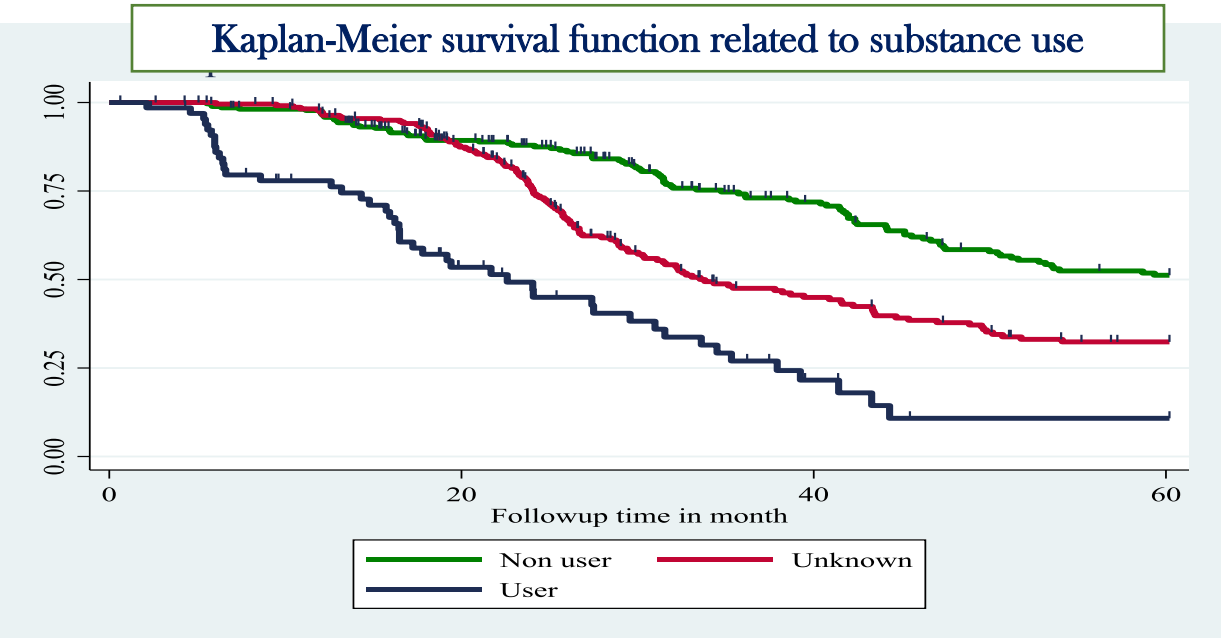

Figure 5: The Kaplan-Meier survival curves compare survival time of ovarian cancer diagnosis with different categories of substance use in TASH and SPHMMC, Addis Ababa, Ethiopia from January 1st 2019 to December 31th 2023.

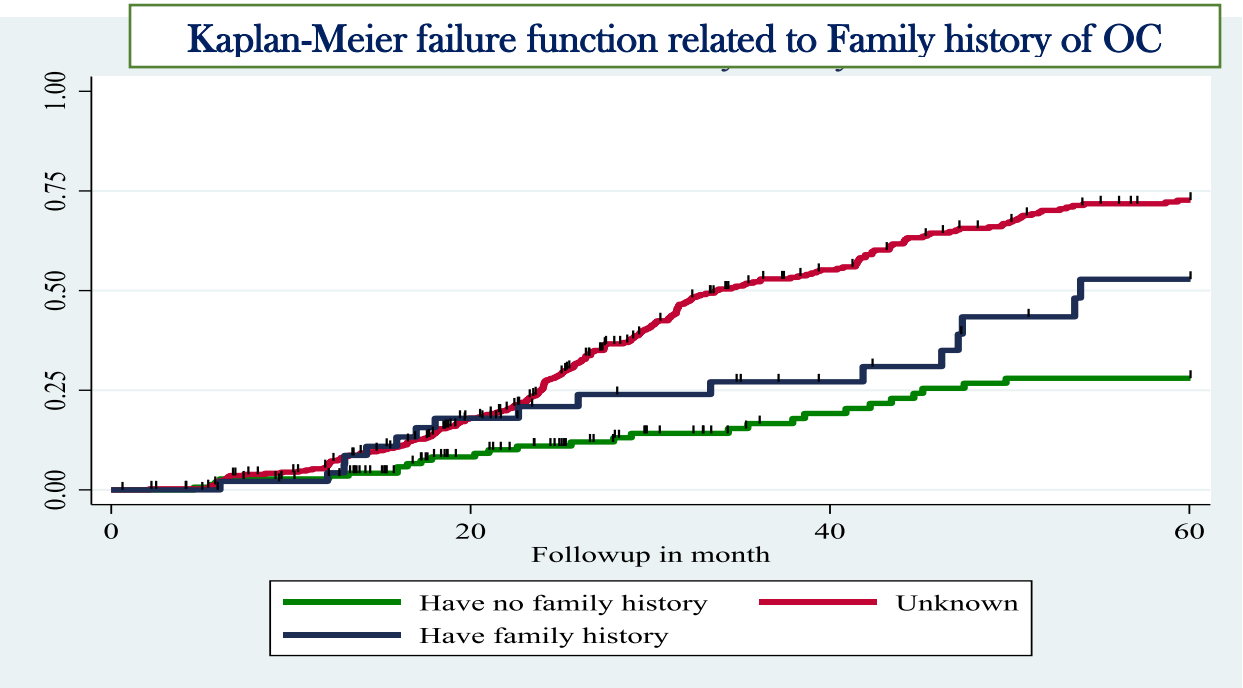

Figure 6: The Kaplan-Meier Hazard curves compare survival time of ovarian cancer diagnosis with different categories of family history of ovarian cancer in TASH and SPHMMC, Addis Ababa, Ethiopia from January 1st 2019 to December 31th 2023.

The Kaplan-Meier graph shows the cumulative 5-year survival for those who use combined oral contraceptives had a higher survival rate (71.06%, 95%CI: 49.81-84.58) than for those who did not use combined oral contraceptives (47.03%, 95%CI: 39.68-54.02). The difference was statistically significant (p-value < 0.001) (Figure 7).

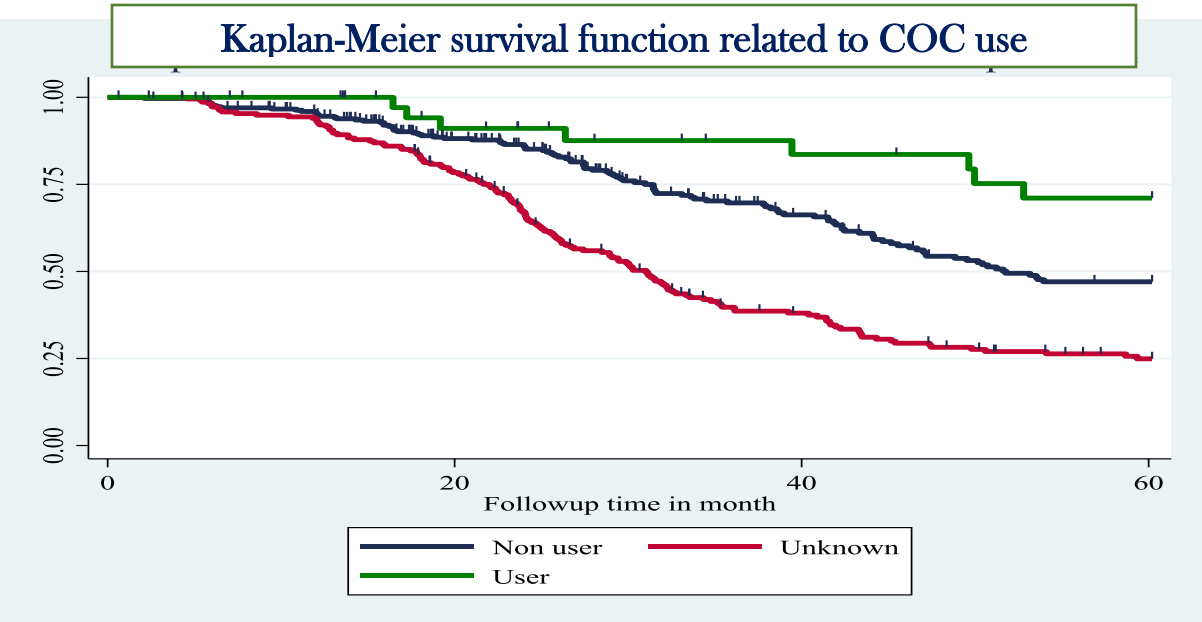

Figure 7: The Kaplan-Meier survival curves compare survival time of ovarian cancer diagnosis with different categories of contraceptive use in TASH and SPHMMC, Addis Ababa, Ethiopia from January 1st 2019 to December 31th 2023.

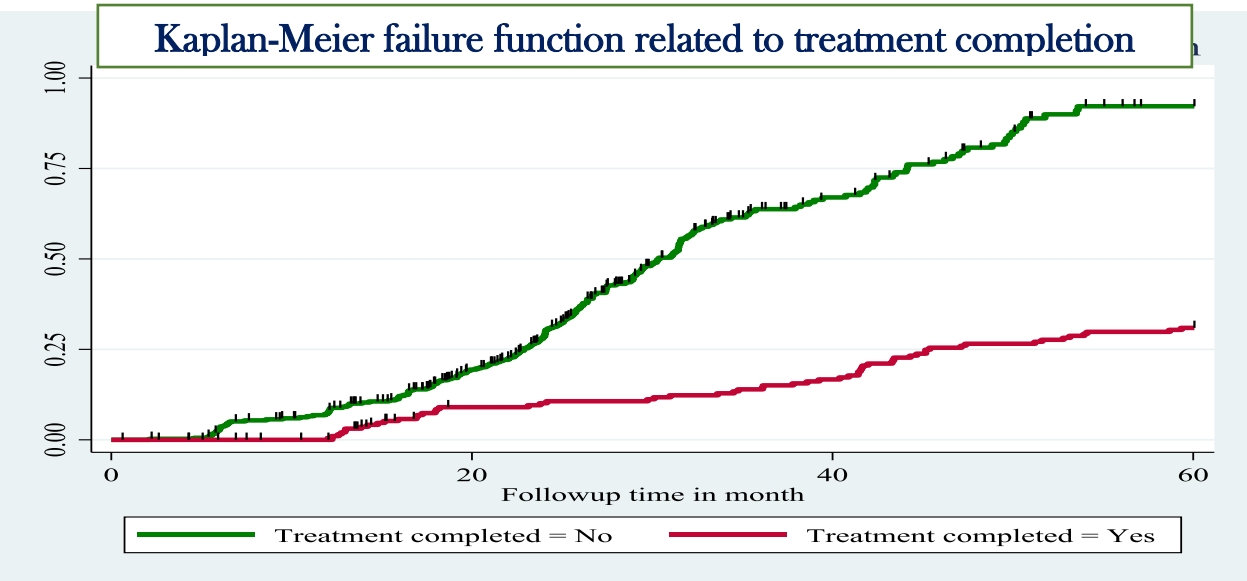

Figure 8: The Kaplan-Meier Hazard curves compare survival time of ovarian cancer diagnosis with different categories of treatment completion in TASH and SPHMMC, Addis Ababa, Ethiopia from January 1st 2019 to December 31th 2023.

The Kaplan-Meier graph shows that the cumulative 5-year survival for premenopausal women had a higher survival rate (64.60%, 95%CI: 51.01-71.94) than postmenopausal women (24.95%, 95%CI: 19.74-30.50). The difference was statistically significant (p-value < 0.001) (Figure 9).

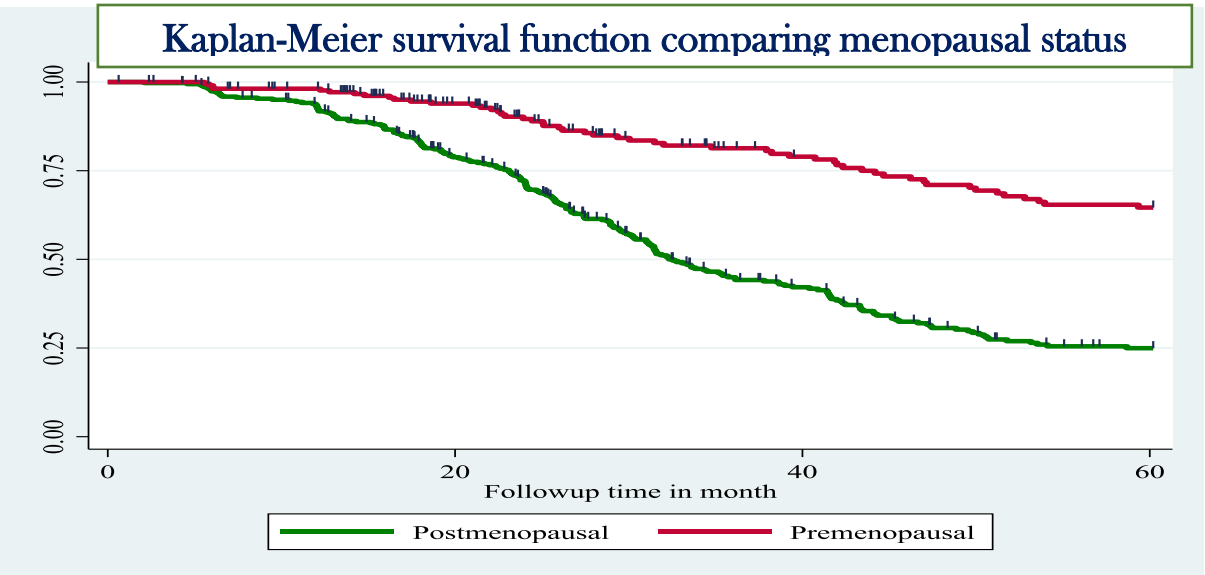

Figure 9: The Kaplan-Meier survival curves compare survival time of ovarian cancer diagnosis with different categories of menopausal status in TASH and SPHMMC, Addis Ababa, Ethiopia from January 1st 2019 to December 31th 2023.

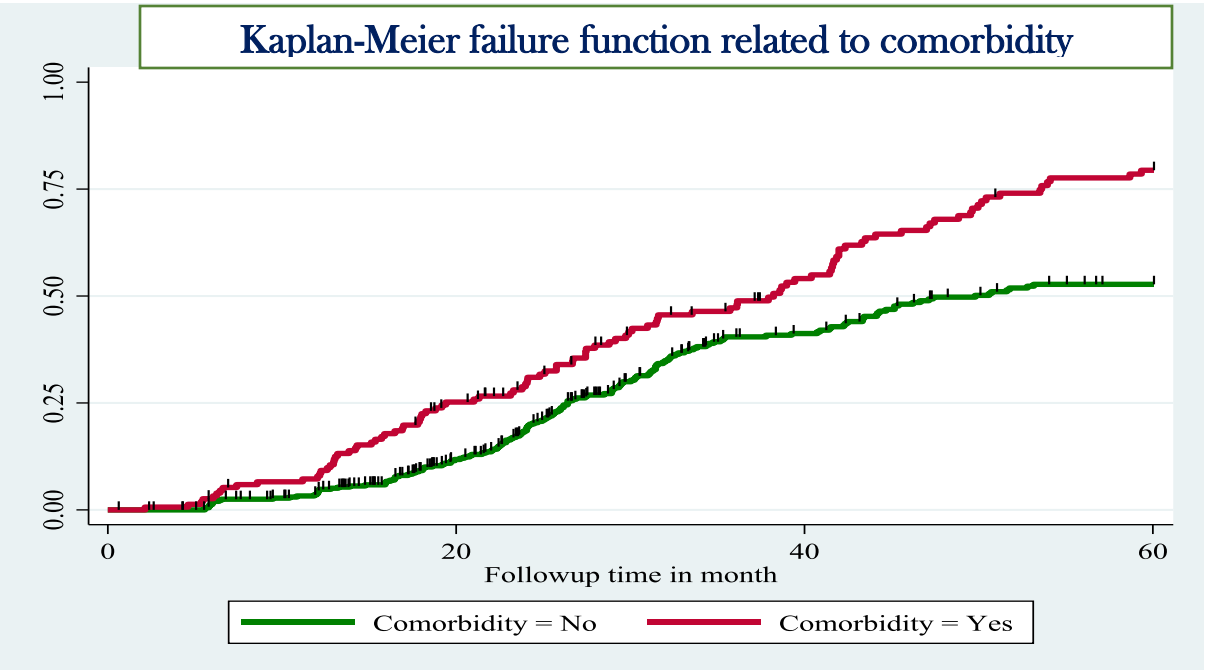

Figure 10: The Kaplan-Meier Hazard curves compare survival time of ovarian cancer diagnosis with different categories of comorbidity in TASH and SPHMMC, Addis Ababa, Ethiopia from January 1st 2019 to December 31th 2023.

5.8. Predictors of ovarian cancer mortality

First, a bivariable Cox proportional Hazard regression model was performed; age at diagnosis, FIGO stage, histology type, pre-existing comorbidity, menopausal status, family history of ovarian cancer, number of parity, treatment completed, combined oral contraceptive user status, treatment mode, and pain medication received were associated with survival status (P <0.2).

Then, multivariable Cox regression analysis was performed by adjusting the effect of confounders using all variables with a p-value of <0.2 in the bivariable analysis and non-collinear explanatory variables. Finally, seven variables were associated with ovarian cancer mortality in the multivariable Cox proportional hazards model.

Multivariable analysis showed that women age over 60 years had a 3.35 times higher risk of death than those under 30 years old[AHR: 3.35; 95%CI: (1.23–9.18)]. Those women with advanced clinical stage (III and IV) at the beginning of ovarian cancer diagnosis were 2.29 times more likely to die as compared to those with early FIGO clinical stage (stage I) [AHR: 2.29, 95%CI: (1.18-4.46)]. Patients with epithelial histologic type of ovarian cancer were 9.67 times more likely to die as compared to those with sex-cord stromal ovarian cancer [AHR: 9.67, 95%CI: (1.32-70.19)].

Ovarian cancer patients who have comorbidity were 1.46 times higher risk of death as compared to patients who have no comorbidity [AHR: 1.46, 95%CI: (1.11-1.93)]. Furthermore, women who did not complete their treatment during the five-year follow-up were 3.09 times more likely to die in comparison to those who completed the given treatment [AHR: 3.09, 95%CI: (2.15-4.47)]. A woman who had palliative care was 7.68 times more likely to die, whereas a woman who had a treatment mode of chemotherapy and surgery together reduced mortality by 64% as compared to a woman who had chemotherapy alone [AHR: 7.68, 95%CI: (2.87-20.52)] and [AHR: 0.36, 95%CI: (0.20-0.64)] respectively.

Combined oral contraceptive user women's reduced mortality by 55%, whereas there was slightly lower protection among non-users (42%), as compared to those women's whose combined oral contraceptive user status were not known [AHR: 0.45, 95%CI: (0.21-0.96)] and [AHR: 0.58, 95%CI: (0.44-0.75)] respectively.

Table 8: Results of the bivariable and multivariable cox regression analysis of ovarian cancer patients at oncology centers, Addis Ababa, Ethiopia, from Jan 1st 2019 to Dec 31th 2023 (n=561).

Covariates	Category	Bivariable CHR (95% CI)	Multivariable AHR (95% CI)	P-value
Age at diagnosis	<30	1	1	
	30-39	1.72(0.79-3.72)	0.78(0.33-1.86)	0.578
	40-49	3.31(1.67-6.54)*	1.25(0.54-2.90)	0.606
	50-59	4.57(2.30-9.07)*	1.91(0.69-5.34)	0.215
	≥60	9.13(4.79-7.39)*	3.35(1.23-9.18)**	0.019
Number of parity	0-1	1	1	
	2-3	1.64(1.14-2.37)*	1.02(0.69-1.53)	0.911
	≥4+	1.92(1.41-2.62)*	0.73(0.51-1.06)	0.095
Menopausal status	Premenopausal	1	1	
	Postmenopausal	3.27(2.41-4.44)*	0.58(0.31-1.05)	0.072
Family history of ovarian cancer	Yes	1	1	
	No	0.49(0.27-0.89)*	0.59(0.31-1.12)	0.106
	Unknown	1.78(1.08-2.91)*	0.94 (0.52-1.70)	0.845
FIGO stage at diagnosis	Stage I	1	1	
	Stage II	1.51(0.74-3.07)	1.59(0.78-3.28)	0.200
	Advanced(III & IV)	7.74(4.19-14.27)*	2.29(1.18-4.46)**	0.015
Histologic type	Sex-cord stromal	1	1	
	Epithelial	23.5(3.29-167.49)*	9.67(1.32-70.79)**	0.025
	Germ cell	3.37(0.39-28.86)	3.92(0.43-35.39)	0.224
	Others	2.51(0.16-40.19)	2.34(0.14-38.21)	0.552
Comorbidity	No	1	1	
	Yes	1.82(1.42-2.33)*	1.46(1.11-1.93)**	0.007
Combined oral contraceptive user status	Unknown	1	1	
	User	0.22(0.11-0.45)*	0.45(0.21-0.96)**	0.039
	Non-user	0.49(0.38-0.62)*	0.58(0.44-0.75)**	<0.001
Treatment mode	Chemotherapy alone	1	1	
	Palliative care	3.22(1.29-8.02)*	7.68(2.87-20.52)**	<0.001
	Chemo & Surgery	0.23(0.13-0.39)*	0.36(0.20-0.64)**	0.001
	Others	0.71(0.31-1.59)	0.89(0.38-2.12)	0.804
Treatment completed	Yes	1	1	
	No	6.13(4.45-8.44)*	3.09(2.15-4.47)**	<0.0001
Receive pain medication	Yes	1	1	
	No	0.55(0.43-0.70)*	0.99(0.74-1.31)	0.928

AHR; adjusted Hazard ratio, CI; confidence interval, CHR: crude hazard ratio, * and ** indicate: significantly associated variables in bivariable and multivariable analysis ($P < 0.05$).

5.9. Testing proportional hazard assumption

A Cox regression model was employed to assess the effects of sociodemographic, reproductive, clinical, histopathological, and treatment-related characteristics of patients from time to death. First, this study had independent observation and censorship. To check the change in hazard function over the given period of time among different categories, it was assessed by using the log-log plot and Kaplan-Meier survival curve. The Schoenfeld residuals test was conducted to assess the significance of the time-dependability nature of a given predictor variables. The result proved that all independent variables included in the model, including the global PH assumption test, satisfied PH assumptions (p-value > 0.10) (Table 8).

Table 9: Schoenfeld residuals test assessing proportional hazards assumption on cox regression analysis of ovarian cancer patients at TASH and SPHMMC, Addis Ababa, Ethiopia, from January 1st 2019 to December 31th 2023 (n=561).

Covariate	Rho	Chi2	df	Prob>chi2
Age at diagnosis	-0.06502	1.12	1	0.2892
Number of parity	0.03464	0.30	1	0.5826
Menopausal status	-0.01172	0.04	1	0.8436
Family history of ovarian cancer	-0.01424	0.06	1	0.8051
FIGO stage at diagnosis	0.01846	0.12	1	0.7250
Histologic type	0.06398	1.08	1	0.2978
Comorbidity	0.00199	0.00	1	0.9747
Contraceptive user status	-0.07508	1.26	1	0.2608
Treatment mode	-0.01619	0.06	1	0.7989
Treatment completed	-0.06928	1.71	1	0.1907
Pain medication received	0.08984	1.87	1	0.1715
Global test		9.34	11	0.5909

- **rho** indicates the correlation coefficient between the residuals and time. df indicates degree of freedom, **chi2** indicates chi square and **Prob>chi2** indicates level of significance

Finally, the goodness of fit of the Cox regression model was verified using the Cox-Snell residual plot. According to the plot conclusion, these residuals should follow a standard censored exponential distribution with a hazard ratio. The Cox-Snell residual plot follows the reference line tangentially, very closely within a 45-degree alignment; this proves the model was good enough to fit the data. In this study, the result revealed that the cox-snell residuals satisfied the overall model fitness test.

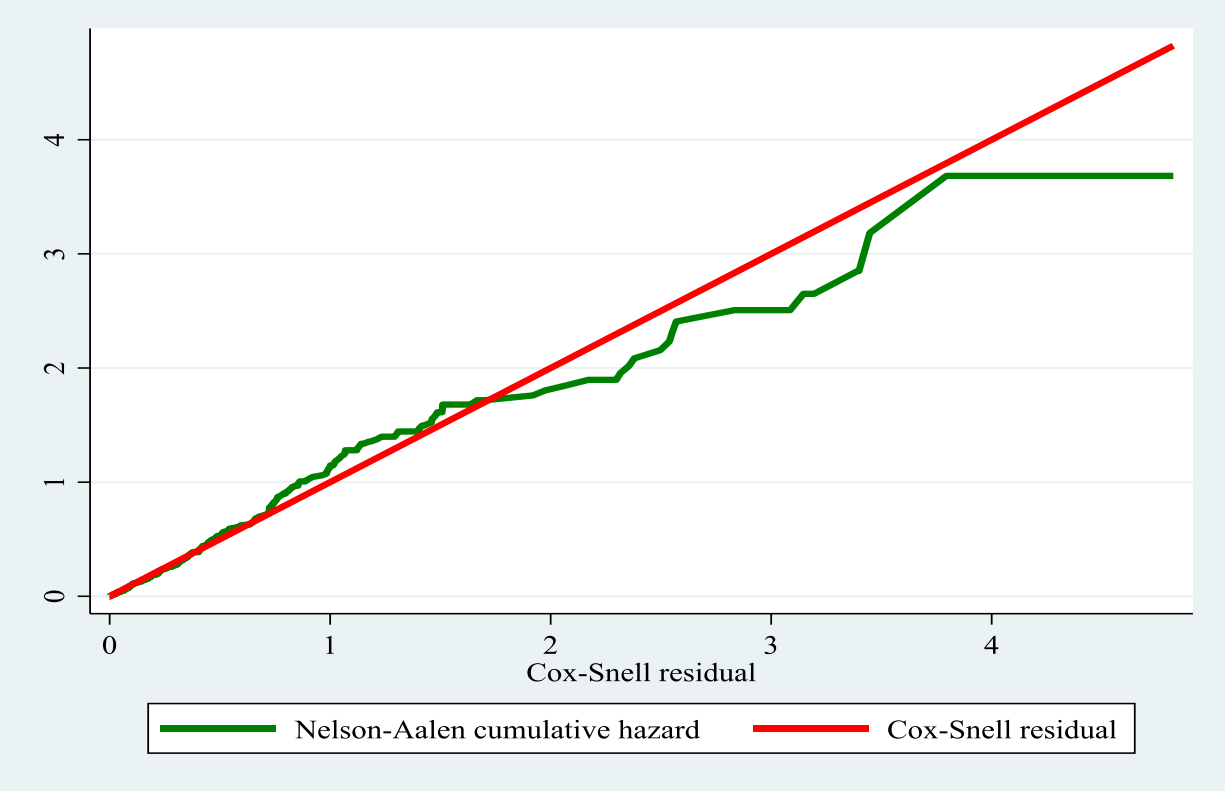

Figure 11: Cox-Snell residual Nelson -Aalen cumulative hazard graph on ovarian cancer patients in TASH and SPHMMC, Addis Ababa, Ethiopia, from January 1st 2019 to December 31th 2023

6. DISCUSSION

This retrospective cohort study was intended to assess the survival status and predictors of ovarian cancer patients at oncology centers in Addis Ababa, Ethiopia. Age at diagnosis, FIGO stage at diagnosis, comorbidities, treatment modality, histologic type, treatment completion, and COC user status were all significant predictors of ovarian cancer survival.

At the end of follow up, the overall mortality of ovarian cancer patients was 264(47.1%) over the five-year study period. This result is slightly greater than a research conducted in Sudan, which is 42%(42). Likewise, the mortality rate for this study is higher than a study done in Iran (13.56%)(38) and Ethiopia (39.3%)(43). On the other hand, the cumulative mortality rate of the present study was in line with the recent studies conducted in Turkey. showed 47.3%(34). This gap could be due to a variety of reasons. One potential cause of variation in mortality rates could be differences in mortality rate estimation, such as in the study conducted in Ethiopia (estimate + uncertainty). Another probable source of variation in the death rate is a difference in sample size, as seen in the Sudan (N=341) and Turkey (N=74) studies.

In this 5-year retrospective follow up study, the overall incidence of mortality of ovarian cancer patients during the 60-month follow up was found to be 16.67 per 100 women-years of observation. This result is substantially greater than what was found in a study in Denmark (13.1 per 100,000)(36) and Alexandria (3.16 per 100,000)(41). This significant disparity could be attributable to a variety of factors, such as late stage at diagnosis and limited access to timely and standard treatment in developing countries(12). Likewise, the observed disparity in mortality rates could be related to the fact that more advanced stage ovarian cancer patients were found in this study. Another potential reason could be the difference in sample size and study period.

In the present study, the overall cumulative survival probability at 12, 24, 36, 48, and 60 months was found to be 95.3%, 78.4%, 57.7%, 44.7%, and 38.9% respectively. This finding was lower than a study that has been conducted in Egypt (96%, 84%, 68%, 54% and 46%)(41). This number remains lower in comparison to studies from high-income countries such as United States, which have 5-year survival rates of 48.6%(37), France (42%)(31) and Iran (61%)(38). Likewise, a systematic review and meta-analysis study conducted in Asian countries revealed that, the survival rates after 5 years were 59.60%(32). However, the overall 5-year survival rate were higher than a study conducted in Senegal (13.3%)(40), Ethiopia (33.9%)(43), Turkey

(25.5%)(34) and Botswana (62.8% and 43.7%) at 1 and 2 years, respectively(30). This finding was consistent with a study conducted in Norway showed that the overall 5-years survival rate was 39%(35), Denmark (40%)(36), and Sudan (38%)(42).

The discrepancy in the results might be due to several reasons, such as a lack of ovarian cancer awareness, a lack of early screening programs and facilities, limited resources, and an increasing number of other critical public health issues in developing countries(22,29). Other explanations related to population growth, aging(life expectancy), and economic constraints are among the reasons for variations in survival among different countries(25,31). An additional rationale could be that cancer treatment facilities are concentrated in the country's capital city; therefore, most cancer patients are referred to the central level, which could result in a delay in diagnosis and treatment. Furthermore, potential reasons for discrepancies in survival include variations in the methodology used in each study, as well as differences in sample compositions based on patient stage and age.

Five year, cumulative survival also differs depending on the stage of ovarian cancer. Our study shows the overall survival of patients diagnosed with FIGO stage I, stage II & advanced (stage III&IV) after 5–years was 80.34%, 71.29% and 17.22% respectively. This result was lower than the study that has been done in France, which is 89%, 70%, 36%, and 17%, for stages I, II III, and IV, respectively(31). Similarly, lower than a study conducted in Egypt, showed that the overall 5-years survival rate for tumors stage I to IV were 85%, 71%, 41% and 22% respectively(41). Patients in the early stages of the disease had a better chance of surviving. This could indicate that early detection and treatment significantly improve the survival rate of ovarian cancer patients. Furthermore, it is possible to conclude that the high mortality rate associated with ovarian cancer is attributed to a lack of public awareness, poor screening, and late stage patient presentation.

The overall median survival time for this study was 43.4(95% CI, 40.39 – 47.37) months. Our findings were higher than the study in Sudan, in which the overall median survival time was 31 months(42) and 32.5 months(estimate + uncertainty) in Ethiopia(43). Although, the present study revealed higher overall median survival time than that seen in Turkey (36 months)(34) and a study done in Norway(32 months)(35). This gap might be, the higher median survival time obtained in comparison with a study in Sudan and Norway is most likely because of the shorter

time of investigation in this study. Additionally, there may be differences in health-seeking behaviour and treatment adherence between those studies. Furthermore, one possible source of variation in median survival time might be a difference in estimation of median survival time, i.e., the study in Ethiopia (estimate + uncertainty), and the difference might be related to sample size, for example, the study in Turkey (N=74).

The log rank test reveals significant variations in survival experience among patients with ovarian cancer based on their baseline characteristics. To assess the equality of the survival curve, Kaplan-Meier analysis of survival status showed that the median survival time for those with clinical stage I or II at baseline had a longer survival time than those in advanced clinical stage (III&IV) (32.27months, 95%CI: 30.09-35.72). The difference was statistically significant (p-value < 0.001). Likewise, women who had no residual tumor after surgery had a longer median survival time than those who had a residual tumor after surgery (35.33months, 95%CI: 30.37-40.29), the difference was statistically significant (p < 0.001). This result is consistent with studies conducted in Turkey, Norway, Egypt, and Sudan (34,35,41,42). The mechanism is that residual tumor tissue after surgery and advanced FIGO stage are the most important predictors or significant factors for ovarian cancer patients, this will eventually lead to death(45).

After confounders adjustment using multivariate Cox proportional regression model, the independent significant predictor of reduced survival in ovarian cancer patients was advanced age at diagnosis, advanced FIGO stage at diagnosis, having comorbid illness, and having epithelial tumor; hence, chemo-surgery treatment modality, COC use, and treatment completed were protective factors.

In our study, patients' age at diagnosis was revealed to be an independent predictor of mortality among ovarian cancer women. Women with advanced age (≥60) had a 3.35 times higher risk of death as compared to those with early age (<30). This finding is consistent with several studies conducted in various countries throughout the world(21,35,36,44–46), in which being a younger patient was an important determinant of survival. This might be due to the fact that comorbidities are more common in elderly women, which can complicate cancer therapy and increase the chance of complications and death(75). Moreover, age-associated decline in physical health (decreased organ function and immunological function) and age-related biological factors makes ovarian cancer more aggressive and resistant to therapy in older patients(76).

According to this study, we found that the advanced FIGO clinical stage (III and IV) of ovarian cancer was found to be a strong predictor of mortality. Those women with advanced clinical stages (III and IV) at the beginning of ovarian cancer diagnosis had a 2.29 times higher risk of death as compared to those with early clinical (stage I). This finding is in agreement with several studies conducted in different developed and developing countries(34,35,41,43–46,52,58), which reflect FIGO stage is an important determinant of survival of ovarian cancer. This could be due to the fact that ovarian cancer symptoms are vague and non-specific, resulting in a delayed diagnosis, and the tumors biological characteristics, such as aggressiveness and resistance to treatment, can also contribute to a higher mortality rate in women with advanced stages(77).

As shown by others, we found that having a comorbid illness was a strong marker of mortality among ovarian cancer patients. Ovarian cancer patients who have comorbidity were 1.46 times increased hazard of death as compared to patients who have no comorbidity. This finding is in line with a study in United States and Norway(35,46), which reflects that comorbidity is an important predictor of mortality among ovarian cancer patients. This could be because comorbidities have an impact on a woman's overall health and immune function, making it more difficult for her body's defence mechanism to fight cancer and recover from therapy. This also increases the chance of life-threatening complications during treatment(75). Moreover, the presence of comorbidities may mask or obscure ovarian cancer symptoms, resulting in delayed detection and treatment. All of this may reduce the likelihood of survival.

In this study, ovarian cancer patients with epithelial-type tumors were a strong predictor of mortality. Patients with epithelial histologic ovarian cancer had a 9.67 times higher risk of death as compared to those patients with sex-cord stromal ovarian cancer. This result is in line with a study in France and Virginia(59,60). The histologic type of ovarian malignancy is an important predictor of survival and has the most significant influence on patient outcome in the present study. This might be due to the nature of epithelial tumor, which is aggressive, heterogeneous, does not cause symptoms in the early stages, and has a higher likelihood of spreading to other parts of the body as compared to other histologic types of ovarian cancer; this can result in a poorer prognosis and a higher mortality rate(78).

In the findings of the present study, combined oral contraceptive user women's mortality was reduced by 55% as compared to those women’s whose combined oral contraceptive user status

was not known. This finding is in agreement with a study in Germany and Toronto, Canada (53,54), which reflects that COC use is an important determinant of the survival of ovarian cancer patients. The exact mechanism by which oral contraceptives cause such profound and long-lasting protection against ovarian cancer is, nevertheless, not well understood. However, the main effects of oral contraceptives are to suppress ovarian activity, so some protection against neoplastic change is plausible. This makes it reasonable to infer that the associations seen here are chiefly causal (i.e., that combined oral contraceptive use decreases the incidence of ovarian cancer mortality)(79).

Finally, treatment mode and treatment completion were found to be independent predictors of survival that became statistically significant in the Cox proportional hazard model.

Those women who did not complete their treatment were found to be a strong predictor of mortality among ovarian cancer patients. Women who did not complete their treatment during the five-year follow-up period had a 3.09 times increase hazard of death as compared to those who completed the given treatment. This finding is in line with different studies(46,63), which reflect that ovarian cancer treatment completion was an important determinant of survival. The possible reason may be incomplete treatment, which allows the disease to worsen and potentially spread to other organs, as well as the development of drug resistance, which makes subsequent treatment unsuccessful. Moreover, untreated or inadequately treated ovarian cancer symptoms can result in a poor quality of life and impairment in overall health that may eventually lead to a higher death rate.

A woman who had palliative care was 7.68 times more likely to die, whereas a woman who had a treatment mode of chemotherapy and surgery together reduced mortality by 64% as compared to a woman who had chemotherapy alone. This finding is in line with Italy and ACOG studies (64,80). The reason for this difference in outcomes is; one probable explanation is that most patients receiving palliative care are in advanced stage of disease, with a poorer prognosis(81). This could explain the greater death rate in this particular category. The combination of chemotherapy and surgery is an effective treatment approach for ovarian cancer(82) and combination treatment could be in a better general health condition and have a less advanced stage of disease. This could be the reason for lowered in mortality rates.

7. LIMITATION AND STRENGTH OF THE STUDY

7.1. Limitation of the study

Our study has some limitations. First, cause-specific (relative) survival was not assessed due to a lack of data on specific causes of mortality, which might overestimate the ovarian cancer-associated death rate. Second, information relating to socioeconomic and reproductive health characteristics such as occupation, educational level, age at menarche, unexplained infertility, age at first birth, and age at menopause were not documented on the chart and not included in this study. Due to the exclusion of incomplete medical files during data collection, selection bias might have been introduced, potentially underestimating or overestimating the mortality rate

The data were collected from charts of ovarian cancer patients diagnosed between January 1st, 2017 and December 31st, 2018; this might not shows the present utilization of refined treatment modalities for ovarian cancer treatment, potentially altering the chance to improve the survival rate. Furthermore, the quality of the data was compromised by the fact that patient medical records were handwritten and stored manually, and documentation was somewhat incomplete.

7.2. Strength of the study

Despite the previously mentioned possible limitations, this study has the following strengths:

The study was conducted in all oncology centers in Addis Ababa, which provide cancer treatment for more than five years; this may increase the generalizability and validity of the study. Nurses who were trained in cancer care, which has a significant impact on the data's quality, collected the data. The research will provide insight for future researchers, particularly for prospective studies. A retrospective cohort study using survival analysis that takes into account time and censoring. Although the result was death, it was easy to determine a temporal relationship with explanatory variables obtained at the time of admission.

8. CONCLUSION

The overall five-year survival rate for patients diagnosed with ovarian cancer was 38.87%, which was lower than that of high- and middle-income countries. Cox proportional hazard analysis revealed that significant predictors of death following ovarian cancer diagnosis were: advanced FIGO stage, epithelial histology, comorbidity, and advanced age. In contrast, chemotherapy and surgery treatment modes, COC users and treatment completion were found to reduce mortality.

9. RECOMMENDATIONS

Based on the findings of this study, the following recommendations could be forwarded to the respective bodies:

To TASH and SPHMMC

- Encourage regular screening for ovarian cancer and enhance access to screening and diagnosis services, particularly for women with risk factors, to early detect the disease and increase survival rates.
- Provide a range of support services, i.e., counselling, support groups, and help manage treatment side effects to decrease the lost to follow-up before treatment completion.
- Enhance treatment using feasible and effective regimens and also increase access to specialized care, including gynaecologic oncologists and other experts in the field.
- Improving healthcare providers' recognition of early signs and symptoms of ovarian cancer and encouraging women to seek clinical support are vital activities.

To healthcare professionals at TASH and SPHMMC

- Healthcare providers' could closely monitor and provide regular follow-up for patients in advanced stages due to the significant death rate among those groups in this study.
- Healthcare professionals should be capable of closely monitoring until the end of treatment and identifying and managing the potential barriers for lost to follow-up because it has been shown to be a preventive predictor for the ovarian cancer death.
- Priority should be given to elderly patients with comorbidities, epithelial types of ovarian tumors, and other identified predictors of death in this study.

To future researchers

- Future researches on ovarian cancer patients' survival status and determinants using a prospective design and developing methodologies that enhance data completeness can address the current study's limitations.
- A longitudinal prospective cohort study is often recommended since it includes important factors of mortality such as socioeconomic status (societal and financial constraints), treatment adherence, and health-care system-related characteristics.
- Further community-based research on the survival status of ovarian cancer patients following censorship is needed to avoid the estimate.

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APPENDIX

ANNEX 1: Information sheet English version

Title of the Research proposal: Survival status and predictors among Ovarian Cancer Patients at Oncology Centers, Addis Ababa, Ethiopia, 2024. A retrospective cohort study

Name of Investigator: Abrham Tesfaye (BSC)

Name of the Organization: Addis Ababa University, College of Health Science, School of Nursing and Midwifery, Department of Midwifery.

Name of the Sponsor: Addis Ababa University

Introduction: This information sheet is prepared for selected Hospitals oncology unit Addis Ababa, Ethiopia. The aim of the form is to make the above concerned office clear about the purpose of research, data collection procedures and get permission to conduct the research.

Purpose of the Research: To assess the survival status and predictors among Ovarian Cancer Patients at Oncology Centers, Addis Ababa, Ethiopia, 2024.

Procedure: In order to achieve the above objective, information, which is necessary for the study, will be taken from ovarian cancer medical record follow up forms, chemotherapy intake forms, radiation therapy chart and medical history sheet. In order to come up with the above mentioned findings, total document of program clients enrolled during January 1st 2017 to December 31th 2018 will be selected and followed up-to December 31th, 2023 and a review of the required information from the records will be made by using the checklist. There will be a phone call to patients to collect information on some variables.

Risk and /or Discomfort: Since the study will be conducted by taking appropriate information from medical chart, it will not inflict any harm on the patients. The name or any other identifying information will not be recorded on the questionnaire and all information taken from the chart will be kept strictly confidential and in a safe place. The information extracted will be kept secured by locked in to locker by key, after the data will be entered in to the computer by password. The information retrieved will only be used for the study purpose.

Benefits: The research has no direct benefit for those whose document/ record is included in this research. However, the indirect benefit of the research for the participant and other clients in the

program is clear. This is because if program planners are preparing predicted plan there is a benefit for clients in the program of getting appropriate care and treatment services for the ovarian cancer patients. Of all, the research work has a paramount direct benefit for health care planners and managers, especially for those on ovarian cancer program planning and management.

Confidentiality: To ensure confidentiality the data on the chart will be collected by those individuals who are working in oncology unit nurse and information will be collected without the name of the clients. The information collected from this research project will be kept confidential and will be stored in a file. In addition, it will not be revealed to anyone except the investigator and it will be kept in key and locked system with computer password.

Person to contact: This research project will be reviewed and approved by the institutional review board of College of Health Sciences, School of Nursing and Midwifery, Addis Ababa University. If in case you want to know more information about the research and its undertakings, you can contact the committee through the address below.

1) Abrham Tesfaye (BSC): Dilla University, College of Health Science, Department of Midwifery. Tel: 0912861405. **E-mail:** abrhamtesfaye95@gmail.com.
2) Jembere Tesfaye (MSC, Assistance Professor): Addis Ababa University, college of health sciences, school of nursing and midwifery. **E-mail:** jembere.tesfaye@aau.edu.et
3) Roza Teshome (MSC, PHD fellow, Assistance Professor): Addis Ababa University, CHS, school of nursing and midwifery. **E-mail:** rozateshome2007@gmail.com

Permission: Lastly but not least, you are kindly requested to permit and forward your permission to concerned body in your organization so that the researchers can get cooperation from the data clerks and other responsible bodies in place.

Thank you for your cooperation

ANNEXES II: Data extraction form of English version

Table 10: Data extraction form for the assessment of survival status and predictors among Ovarian Cancer Patients at Oncology Centers, Addis Ababa, Ethiopia, January 1st 2019-December31th 2023.

Part I: Socio Demographic and Reproductive Health Characteristics			
1.	Identification number	_ _ _ _ _ _ _ _ _	
2.	Patient age at diagnosis	----------year	
3.	Marital status	1) Single 2) Married	
4.	Region	1) Addis Ababa 2) Amhara 3) Oromia 4) Tigray 5) SNNP 6) Others (specify…...)	
5.	Occupation	1) Government employee 2) Merchant 3) Farmer 4) Student 5) Private employee 6) Daily labourer 7) Unknown	
6.	Substance use	1) User 2) Non user	
7.	Parity	_____	
8.	Menopausal status	1) Premenopausal 2) Postmenopausal	
9.	Contraceptive use (COC)	1) Yes 2) No 3) Unknown	
10.	HIV status	1) Positive 2) Negative 3) Unknown	

11.	Family History of Ovarian Cancer	1) Yes 2) No 3) Unknown	
Part Two:- Clinical and Histopathological Variable			
1.	Date of ovarian cancer diagnosis	---------/----------/--------	
2.	Stage of cancer at diagnosis	1) _____ 2) Unknown	
3.	Histology type of ovarian cancer	1) Epithelial, 2) Germ cell, 3) Sex cord-stromal, 4) Borderline, 5) Cytology only/no pathology	
4.	Baseline Haemoglobin	_____	
5.	Comorbidity	1) Yes (specify…...) 2) No	
6.	If yes on Question 5 specify type of comorbidity	_____	
7.	Metastasis at time of diagnosis	1) Yes 2) No	
8.	CA-125 elevated (cut off35unit/ml)	1) Yes 2) No 3) Unknown	
9.	Chief compliant of the patient	1) Abdominal distension/mass 2) Abdominal pain 3) Vaginal bleeding 4) Weight loss 5) Preoperative ascites 6) Other (Specify ___)	
Part three: Treatment related variable			
1.	The primary treatment initiated	1) Surgery 2) Radiotherapy 3) Chemotherapy 4) Chemo-Radiotherapy 5) Surgery + Radiotherapy and	

		chemotherapy 6) Palliative care	
2.	Duration of treatment	_____	
3.	If chemotherapy, how many cycles	_____	
4.	If radiotherapy total dose of irradiation (Number of rounds)	_____	
5.	If surgery, presence of residual tumor	1) Yes 2) No 3) Unknown	
6.	Treatment completed	1) Yes 2) No	
7.	Date of treatment initiated	_____	
8.	Waiting time (from the date of diagnosis to treatment date)	_____	
9.	Pain medication received	1) Yes 2) No	
10.	Status of the patient during last contact	1) Death 2) Alive 3) Lost to follow up, 4) Transfer to and against medical advice	
11.	If dead, lost to follow up, transfer to or alive when last date of contact	____/____/____	
	Data extractor name Abstraction date	---------- ----------/-------/--------	

ANNEX III: Revised FIGO Staging

The International Federation of Gynecology and Obstetrics (FIGO) revised ovarian cancer staging system

Stage 1

- **Stage 1A:** Tumor is limited to one ovary or fallopian tube
- **Stage 1B:** Tumor is limited to both ovary or fallopian tube
- **Stage 1C:** Malignant cell found on ascites or peritoneal washing

Stage II

- **Stage IIA:** Tumor extended to or is implanted on uterus or fallopian tube
- **Stage IIB:** Tumor extended to or is implanted on both uterus and fallopian tube and extended to other intraperitoneal tissue (below the pelvic brim).

Stage III

- **Stage IIIA:** Tumor involvement exclusively on retroperitoneal lymph node.
  - **Stage $IIIA_1$:** in which metastasis is 10mm or smaller in greatest dimension.
  - **Stage $IIIA_2$:** in which metastasis is larger than 10mm in greatest dimension.
- **Stage IIIB:** Microscopic extrapelvic (above pelvic brim) peritoneal involvement is seen with or without positive retroperitoneal lymph node(≤2cm)
- **Stage IIIC:** Microscopic extrapelvic (above pelvic brim) peritoneal involvement is seen with or without positive retroperitoneal lymph node(>2cm)

Stage IV

- **Stage IVA:** indicates pleural effusion with positive cytology
- **Stage IVB:** Hepatic or splenic parenchymal metastasis is seen or both, as well as metastasis to extra abdominal organs.

ANNEX IV: Comorbidities

The Charlson comorbidity index

Each condition is assigned with a score of 1, 2, 3 or 6 depending on the risk of dying associated with this condition.

Disease conditions:

Acute Myocardial Infarction

Congestive Heart Failure

Peripheral Vascular Disease

Cerebrovascular Disease

Dementia

Chronic Obstructive Pulmonary Disease

or other Respiratory diseases

Rheumatic-like Diseases

Ulcers of the Digestive System

Liver Disease – Mild

Diabetes - No Chronic Complications

Diabetes with Chronic Complications

Hemiplegia or Paraplegia

Renal (Kidney) Disease

Cancer (No secondary found)

Liver Disease - Moderate or Severe

Cancer (Metastatic - secondary)

HIV / AIDS

SURVIVAL STATUS AND PREDICTORS AMONG OVARIAN CANCER PATIENTS AT ONCOLOGY CENTERS, ADDIS ABABA, ETHIOPIA, 2024

ORIGINALITY REPORT

15%	17%	11%	2%
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