



Clinical Characteristics and Risk Factors of Patients with Epithelial Ovarian Cancer

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ABSTRACT

Epithelial ovarian cancer is a major cause of gynecological cancer-related morbidity and mortality. Several factors, including age, parity, contraceptive use, and family history, have been reported to influence the risk of ovarian cancer. This study aimed to describe the characteristics of patients with epithelial ovarian cancer treated at Tarakan Regional General Hospital, Jakarta, and to examine the association of epithelial ovarian cancer with age, parity, contraceptive use, and family history. This observational analytic study used a cross-sectional design and secondary data obtained from the medical records of patients treated between 2018 and 2022. A total of 50 eligible patients were included using a total sampling technique. Data were analyzed using the chi-square test. Most patients were aged >50 years (58.0%), had a parity of ≥ 1 (98.0%), had not used contraception (76.0%), and had no family history of ovarian cancer (92.0%). Chi-square analysis showed no statistically significant associations between age ($p = 0.069$), parity ($p = 0.465$), contraceptive use ($p = 0.326$), or family history ($p = 0.637$) and epithelial ovarian cancer. The majority of patients with epithelial ovarian cancer were aged >50 years, had given birth at least once, had no history of contraceptive use, and had no family history of ovarian cancer. Further studies involving larger sample sizes and an appropriate comparison group are needed to better investigate potential risk factors for epithelial ovarian cancer.

INTRODUCTION

Ovarian cancer is one of the most important gynaecological malignancies worldwide because it is frequently diagnosed at an advanced stage and is associated with substantial mortality. Ovarian tumours comprise benign, borderline, and malignant neoplasms, with malignant tumours contributing significantly to deaths from gynaecological cancers. The disease may present with few or nonspecific symptoms during its early stages, resulting in delayed diagnosis and contributing to its characterization as a “silent killer.” Therefore, identification of factors associated with ovarian cancer is important for improving recognition of women at increased risk (World Health Organization, 2017; Prawirohardjo, 2010).

Ovarian cancer also represents an important public health concern in Indonesia. Data cited by the Indonesian Network of Gynaecologic Oncology (INASGO) for 2015–2019 reported approximately 6,500 new ovarian cancer cases and 4,400 deaths annually in Indonesia (INASGO, 2015–2019). The burden of disease highlights the importance of understanding the characteristics of patients with ovarian cancer and the factors potentially associated with its occurrence.

Several demographic, reproductive, contraceptive, and hereditary factors have been investigated in relation to ovarian cancer. Age, parity, contraceptive use, and family history are among the factors that may contribute to differences in ovarian cancer risk. However, the strength and direction of these associations may vary among populations and healthcare settings. Furthermore, epithelial ovarian cancer is a heterogeneous group of tumours with differences in histopathological characteristics and biological behaviour (Kurman & Shih, 2010).

Although previous studies have examined risk factors for ovarian cancer, hospital-based data from Indonesia remain important because differences in demographic and reproductive characteristics may influence the observed distribution of risk factors. Local data may therefore provide useful information regarding the characteristics of patients presenting with epithelial ovarian cancer in specific healthcare settings.

The present study was conducted at Tarakan Regional General Hospital, Jakarta, using medical record data from 2018 to 2022. This study aimed to determine the characteristics of patients with epithelial ovarian cancer and to examine the relationships of age, parity, contraceptive use, and family history with epithelial ovarian cancer characteristics. The findings are expected to provide additional hospital-based evidence regarding epithelial ovarian cancer in Indonesia and serve as a basis for further research involving larger and more diverse populations.

LITERATURE REVIEW

Epithelial Ovarian Cancer

Ovarian cancer represents a heterogeneous group of malignancies that can be classified according to their histogenesis and histopathological characteristics. Epithelial ovarian cancer is the predominant category of ovarian malignancy and comprises several histological subtypes, including high-grade serous, low-grade serous, endometrioid, clear cell, and mucinous carcinomas. Differences among

these subtypes reflect distinct biological pathways and clinical behavior. Consequently, ovarian cancer should not be considered a single uniform disease entity when evaluating potential risk factors (Kurman & Shih, 2010).

Age

Age is an important factor associated with ovarian cancer. The incidence of ovarian cancer generally increases with advancing age, and women in the postmenopausal period represent an important population affected by the disease. The association between increasing age and ovarian cancer has been proposed to involve cumulative genetic and cellular alterations occurring over time, as well as prolonged exposure to ovulatory cycles. Repeated ovulation has historically been proposed to cause recurrent epithelial injury and repair, potentially contributing to the accumulation of cellular abnormalities (Nurlailiyani, 2013; Tortorella et al., 2017).

The relationship between age and ovarian cancer is also influenced by tumor subtype. Certain epithelial ovarian cancer subtypes demonstrate different age distributions and biological characteristics. Therefore, evaluation of age among patients with epithelial ovarian cancer may provide useful information regarding the demographic characteristics of the affected population.

Parity

Parity has been extensively investigated as a reproductive factor associated with ovarian cancer risk. Pregnancy is associated with temporary suppression of ovulation and therefore has been proposed as a potential protective factor against ovarian cancer. The hypothesis is consistent with the concept that a reduction in the lifetime number of ovulatory cycles may decrease repeated epithelial injury to the ovarian surface or related tissues.

Epidemiological studies have generally reported an inverse association between parity and ovarian cancer risk, although the magnitude of this association may differ according to population characteristics and tumor subtype. The relationship is therefore not necessarily consistent across all populations or histological categories (Sung et al., 2016; Wentzensen et al., 2016). Assessment of parity remains relevant when evaluating the reproductive characteristics of women diagnosed with epithelial ovarian cancer.

Contraceptive Use

Contraceptive use, particularly oral contraceptive use, has been associated with ovarian cancer risk. Combined oral contraceptives suppress ovulation, and the reduction in the number of ovulatory cycles has been proposed as one mechanism underlying their potential protective effect. Epidemiological evidence has demonstrated that women who have used oral contraceptives may have a lower risk of ovarian cancer compared with women who have never used them. The protective effect may also increase with longer duration of use (Tsilidis et al., 2011).

The association between contraceptive use and ovarian cancer may vary according to the type and duration of contraceptive exposure and potentially according to tumor subtype. Consequently, contraceptive history is an important reproductive characteristic to consider when examining ovarian cancer risk.

Family History

Family history is another important factor in the assessment of ovarian cancer risk. A proportion of ovarian cancers is associated with hereditary susceptibility, particularly in families with pathogenic variants affecting genes involved in DNA repair and tumor suppression. Familial susceptibility may influence both the likelihood of developing ovarian cancer and the age at which the disease is diagnosed.

The contribution of family history may also vary according to patient age and histological characteristics. Therefore, obtaining information regarding a family history of ovarian or related cancers may provide clinically relevant information when evaluating patients with epithelial ovarian cancer (Zheng et al., 2018).

Relationship Between Risk Factors and Epithelial Ovarian Cancer

Age, parity, contraceptive use, and family history represent distinct but potentially interrelated demographic, reproductive, and hereditary factors associated with epithelial ovarian cancer. Their effects may differ according to the biological characteristics of individual tumors and the population being studied. The heterogeneous nature of epithelial ovarian cancer further indicates that associations observed in one population may not necessarily apply to another population (Kurman & Shih, 2010).

Therefore, evaluating these factors in a specific hospital population may provide useful information regarding the characteristics of women diagnosed with epithelial ovarian cancer. Hospital-based studies can describe the distribution of demographic and reproductive factors among affected patients and may identify patterns that warrant further investigation in larger analytical studies.

Incessant Ovulation Theory

The incessant ovulation theory explains that repeated ovulation may contribute to the development of epithelial ovarian cancer through recurrent injury to the ovarian surface epithelium. Repeated disruption of the epithelial surface requires continuous repair and may increase the possibility of metaplasia, genetic alterations, and subsequent neoplastic transformation. The risk is theoretically influenced by the cumulative number of ovulatory cycles over a woman's lifetime. Increasing age may therefore be associated with prolonged exposure to repeated ovulation and epithelial injury (Kurman & Shih, 2010). The theoretical framework in the original study also links age, parity, menarche, marital status, and contraceptive use with ovarian epithelial injury during ovulation.

Previous findings, however, do not consistently support this theoretical relationship. Simamora, Hanriko, and Sari (2018) investigated age and parity in relation to the histopathological degree of ovarian cancer, while Dheanisa et al. (2019) reported no significant relationship between age and epithelial ovarian cancer. The original study likewise found no significant association between age and epithelial ovarian cancer characteristics ($p = 0.069$). These findings show that age, alone, should not be interpreted as a direct measure of the number of ovulations but a longer reproductive lifespan may result in greater cumulative exposure to ovulatory cycles. In this context, age may serve as an indicator of cumulative reproductive and ovulatory exposure.

Gonadotropin and Reproductive Theory

The gonadotropin and reproductive theory proposes that reproductive events influence ovarian cancer risk through changes in ovulation and hormonal exposure. Pregnancy and childbirth temporarily suppress ovulation, allowing the ovarian epithelium to undergo a period of reduced proliferative activity and repair. Consequently, higher parity is theoretically associated with a lower risk of epithelial ovarian cancer. The study's theoretical discussion states that the protective effect may increase with the number of pregnancies because repeated periods without ovulation provide greater opportunities for epithelial recovery. This hypothesis is supported by Sung et al. (2016), whose systematic review and meta-analysis examined breastfeeding duration and parity in relation to epithelial ovarian cancer. The original study also cites evidence indicating that women who have previously given birth may have a lower risk than nulliparous women. However, findings from Indonesian studies are not completely consistent. Rian et al. and Fachlevy et al. reported no significant association between parity and epithelial ovarian cancer.

Hormonal Contraception and Ovulation Suppression Theory

Hormonal contraception, particularly oral contraceptives, may influence ovarian cancer risk by suppressing ovulation and consequently reducing repeated injury to the ovarian epithelium. According to the theoretical discussion in the original study, oral contraceptive use is associated with a lower risk of ovarian cancer, and longer duration of use may provide greater protection. The study cites evidence that prolonged oral contraceptive use may substantially reduce ovarian cancer risk (Tsilidis et al., 2011).

The epidemiological evidence cited in the original study includes Tsilidis et al. (2011), who examined oral contraceptive use and reproductive factors in relation to ovarian cancer risk, as well as other studies concerning hormonal contraception. Nevertheless, the relationship may depend on the type, duration, and consistency of contraceptive use. The original study notes that these factors may explain differences between studies.

H3: Contraceptive use is significantly associated with the characteristics/degree of epithelial ovarian cancer.

Genetic Susceptibility and Hereditary Theory

The genetic susceptibility theory proposes that hereditary factors may increase susceptibility to epithelial ovarian cancer through inherited mutations affecting DNA repair mechanisms. The original theoretical framework specifically identifies BRCA1/BRCA2 mutations as an important pathway through which hereditary susceptibility may contribute to ovarian cancer development. The study further explains that BRCA mutations may impair the detection and repair of cellular DNA damage, thereby increasing the possibility of malignant transformation.

Previous literature cited in the study indicates that family history is particularly relevant to certain epithelial ovarian cancer subtypes, especially high-grade serous carcinoma. However, hereditary factors do not necessarily influence all epithelial ovarian cancer subtypes to the same extent. This may

explain why the relationship between family history and epithelial ovarian cancer characteristics is not always statistically significant.

Previous Studies and Hypothesis Development

The theoretical and empirical evidence indicates that age, parity, contraceptive use, and hereditary factors may influence epithelial ovarian cancer through different biological pathways. The original research was designed to examine these four factors in patients treated at Tarakan Regional General Hospital, Jakarta, during 2018–2022. The study used an observational analytic cross-sectional design and included 50 patients using total sampling.

Importantly, the previous evidence is not uniform. Theories of repeated ovulation, reproductive protection, hormonal contraception, and genetic susceptibility provide biological justification for the proposed relationships, whereas several empirical studies have reported weak or nonsignificant associations. For example, Simamora et al. (2018) and Dheanisa et al. (2019) provide evidence relevant to age and ovarian cancer characteristics, while Rian et al. and Fachlevy et al. reported no significant association between parity and epithelial ovarian cancer.

The present study therefore tests whether the theoretically expected relationships are observable in the specific population of patients with epithelial ovarian cancer at Tarakan Regional General Hospital, Jakarta. This local hospital-based context provides an empirical contribution because the results can be compared with findings from other Indonesian hospitals.

Hypotheses

Based on the original study's formulation of the hypotheses, which included both null and alternative hypotheses concerning age, parity, contraceptive use, and hereditary factors, these are our hypotheses:

H1: Age is associated with the characteristics/degree of epithelial ovarian cancer.

H2: Parity is associated with the characteristics/degree of epithelial ovarian cancer.

H3: Contraceptive use is associated with the characteristics/degree of epithelial ovarian cancer.

H4: Family history is associated with the characteristics/degree of epithelial ovarian cancer

Conceptual Framework

Based on the theoretical review, the conceptual framework positions age, parity, contraceptive use, and family history as independent variables and epithelial ovarian cancer characteristics/degree as the dependent variable. The conceptual framework of the study is therefore presented as follows

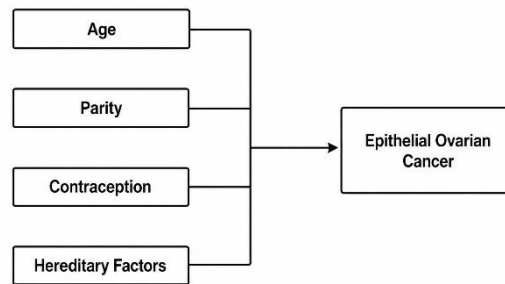


Figure 1. Conceptual Framework

METHODOLOGY

This study employed an observational analytic cross-sectional design to examine the associations between age, parity, contraceptive use, family history, and the characteristics of epithelial ovarian cancer. Secondary data were obtained from patients' medical records and the archives of the Anatomical Pathology Laboratory at Tarakan Regional General Hospital, Jakarta, covering patients diagnosed with epithelial ovarian cancer during 2018–2022. A total of 50 eligible patients were included using total sampling based on predefined inclusion and exclusion criteria. Data were analysed using descriptive and bivariate analyses. Associations between variables were assessed using the Chi-square test, with statistical significance set at $p < 0.05$.

RESULTS AND DISCUSSION

This study was conducted using data from patients with epithelial ovarian cancer who underwent histopathological examination at Tarakan Hospital, Jakarta, between January 2018 and December 2022. Patient data were obtained from the archives of the Anatomical Pathology Laboratory. Eligible patients were identified based on the predefined inclusion and exclusion criteria. The collected data were used to assess the variables examined in this study, including age, parity, contraceptive use, family history, histopathological type, and histopathological grade.

Patient Characteristics

Table 1. Patient Characteristics

Variable	<i>f</i>	%
Age		
≤50	21	42,0
>50	29	58,0
Total	50	100,0
Genetic Factors		
There isn't any	46	92,0
There is	4	8,0
Total	50	100,0
Parity		
0	1	2,0
≥1	49	98,0

Total	50	100,0
Contraception		
Do not use	38	76,0
Use	12	24,0
Total	50	100,0
Histopathological Type		
Clear-Cell Tumor	9	18,0
Serous Tumor	16	32,0
Mucinous Tumor	8	16,0
Endometrioid	17	34,0
Total	50	100,0

Patient Characteristics by Age

Based on Table 2, among the 50 ovarian cancer patients examined, 21 patients were aged ≤ 50 years, accounting for 42.0%, while 29 patients were aged >50 years, accounting for 58.0%. These findings indicate that the majority of ovarian cancer patients in this study were over 50 years of age.

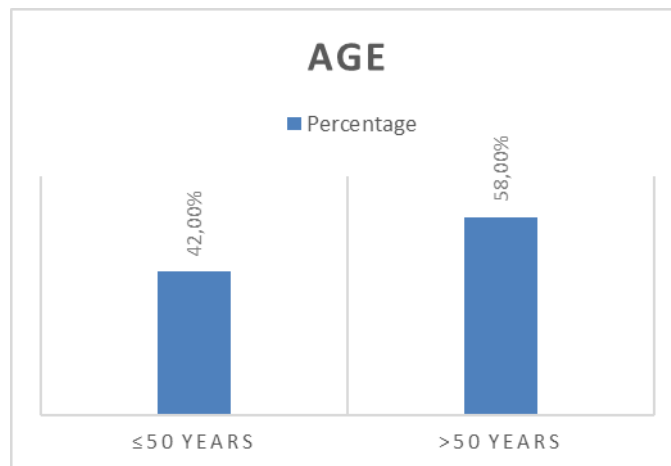


Figure 1. Comparison of Patient Ages

Patient Characteristics Based on Parity

Of the 50 ovarian cancer patients included in the study, one patient had a parity of 0, accounting for 2.0%. In contrast, 49 patients had a parity of ≥ 1 , accounting for 98.0%. Based on these findings, the majority of women with ovarian cancer had a history of at least one childbirth.

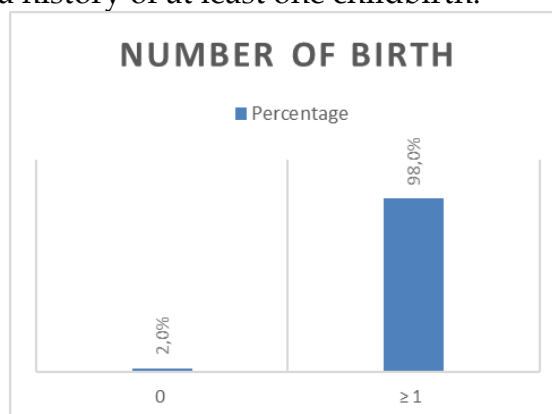


Figure 2. Parity of Respondents

Patient Characteristics Based on Contraceptive Use

Of the 50 ovarian cancer patients included in the study, 38 patients (76.0%) reported not using any form of contraception, while 12 patients (24.0%) reported using contraception. Based on these findings, the majority of patients with ovarian cancer did not use any form of contraception.

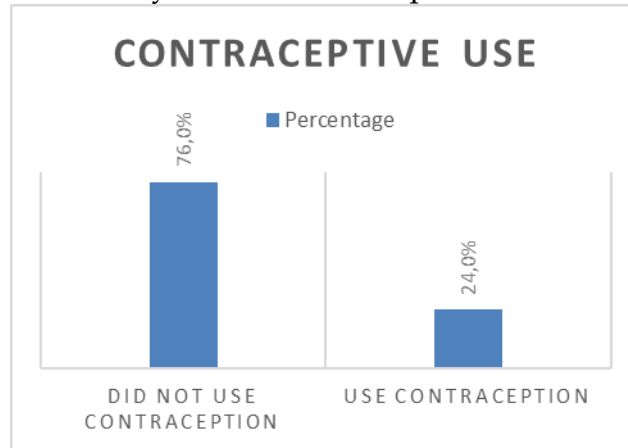


Figure 3. Comparison of Contraceptive Use Among Respondents

Patient Characteristics Based on Family History

Table 4 shows that, among the 50 ovarian cancer patients included in the study, 46 patients (92.0%) had no family history of cancer, while 4 patients (8.0%) had a family history of cancer. Based on these findings, the majority of patients diagnosed with ovarian cancer had no family history of the disease.

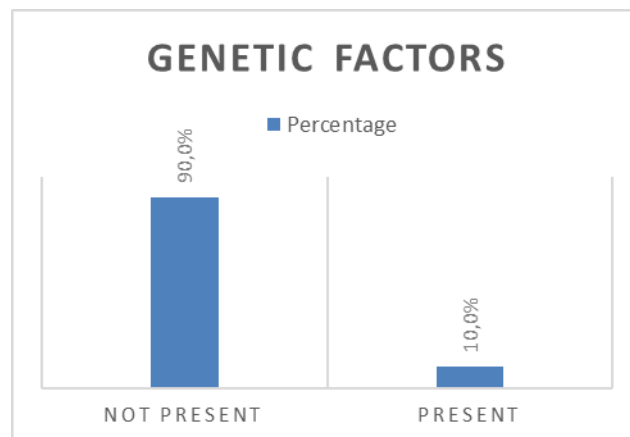


Figure 4. Respondents' Hereditary Factors

Patient Characteristics Based on Epithelial Ovarian Cancer Type

Figure 5 shows that endometrioid tumors were the most common histopathological type, followed by serous, clear cell, and mucinous tumors among the ovarian cancer patients studied.

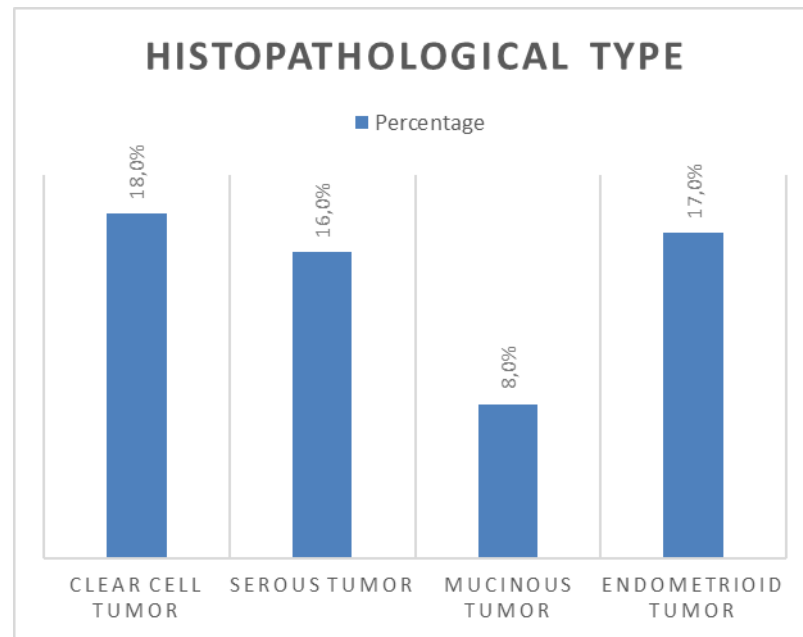


Figure 5. Histopathological Type Description

Association between Age and the Incidence of Epithelial Ovarian Cancer

Table 2. Association between Age and the Incidence of Epithelial Ovarian Cancer

Epithelial Ovarian Cancer					
Age	Bad	currently	Good	Total	<i>p-value</i>
≤50	8	1	12	21	0,069
>50	15	6	8	29	
Total	23	7	20	50	

Among patients with epithelial ovarian cancer, histological differentiation varied across age groups. Chi-square analysis showed no statistically significant association between age and histological differentiation at Tarakan Hospital, Jakarta, during 2018–2022.

The Relationship Between Parity and the Incidence of Epithelial Ovarian Cancer

Table 3. The Relationship Between Parity and the Incidence of Epithelial Ovarian Cancer

Epithelial Ovarian Cancer					
Parity	Bad	currently	Good	Total	<i>p-value</i>
0 Parity	0	0	1	1	0,465
≥1 Parity	23	7	19	49	
Total	23	7	20	50	

Table 3 shows that most patients had a parity of at least one, and parity was not significantly associated with epithelial ovarian cancer differentiation at Tarakan Hospital, Jakarta, during 2018–2022.

The Relationship Between Contraception and the Incidence of Epithelial Ovarian Cancer

Table 4. The Relationship Between Contraception and the Incidence of Epithelial Ovarian Cancer

Epithelial Ovarian Cancer					
Contraception	Bad	currently	Good	Total	<i>p-value</i>
Do not use	19	6	13	38	0.326
Use	4	1	7	12	
Total	23	7	20	50	

Table 4 shows that most patients had never used contraception, and contraceptive use was not significantly associated with epithelial ovarian cancer differentiation at Tarakan Hospital, Jakarta, during 2018–2022.

The Association Between Hereditary Factors and the Incidence of Epithelial Ovarian Cancer

Table 5. The Association Between Hereditary Factors and the Incidence of Epithelial Ovarian Cancer

Epithelial Ovarian Cancer					
Hereditary Factors	Bad	currently	Good	Total	<i>p-value</i>
There isn't any	22	6	18	46	0,637
There is	1	1	2	4	
Total	23	7	20	50	

Table 5 shows that most patients had no family history of cancer, and family history was not significantly associated with epithelial ovarian cancer differentiation at Tarakan Hospital, Jakarta, during 2018–2022.

The findings of this study indicate that age, parity, contraceptive use, and family history were not significantly associated with the histopathological characteristics of epithelial ovarian cancer among patients at Tarakan Regional General Hospital, Jakarta. These findings suggest that the histopathological characteristics of epithelial ovarian cancer may involve complex interactions among reproductive, hormonal, genetic, and biological factors rather than being determined by a single demographic or reproductive factor.

In this study, patients aged >50 years represented the majority of cases (58.0%). Increasing age is generally recognized as an important characteristic of ovarian cancer, as the incidence of the disease tends to increase with age. The incessant ovulation hypothesis proposes that repeated ovulation may result in recurrent epithelial injury and repair, potentially increasing the opportunity for cellular abnormalities and neoplastic transformation. However, the relationship between age and ovarian cancer may also be influenced by reproductive lifespan, age at menarche and menopause, hormonal exposure, and tumor subtype. In the present study, age was not significantly associated with the histopathological characteristics of epithelial ovarian cancer. This finding is consistent with previous studies by Simamora et al. and Nofia et al., which also reported no significant association between age and ovarian cancer characteristics.

Parity was also not significantly associated with the histopathological characteristics of epithelial ovarian cancer in this study. Pregnancy and childbirth have traditionally been considered potentially protective against ovarian cancer because pregnancy suppresses ovulation and consequently reduces the cumulative number of ovulatory cycles. However, parity alone may not adequately represent the complex reproductive mechanisms involved in ovarian carcinogenesis. Other reproductive factors, including age at first pregnancy, number of pregnancies, breastfeeding, age at menarche, age at menopause, and cumulative ovulatory exposure, may influence the observed association. The predominance of patients with parity ≥ 1 in the present study may also have limited the ability to detect differences between nulliparous and parous patients.

Similarly, contraceptive use was not associated with epithelial ovarian cancer characteristics. The effect of contraception may vary according to its type, duration, and hormonal composition. Hormonal contraception may reduce ovulation, but variations in exposure could produce different biological effects. Therefore, a simple classification of contraceptive use may not fully explain its relationship with ovarian cancer. Hereditary factors also showed no significant association in this population. Nevertheless, genetic susceptibility remains important, particularly mutations involving BRCA1 and BRCA2, which are strongly associated with certain ovarian cancer subtypes, especially high-grade serous carcinoma. This suggests that hereditary risk may differ across histopathological subtypes rather than affecting all epithelial ovarian cancers equally. Overall, the findings support the multifactorial nature of epithelial ovarian cancer. Future studies should involve larger populations and include detailed reproductive, hormonal, histopathological, and genetic information to better identify factors associated with specific epithelial ovarian cancer subtypes.

Similarly, contraceptive use was not significantly associated with the histopathological characteristics of epithelial ovarian cancer. Hormonal contraceptives, particularly oral contraceptives, have been associated with a reduced risk of ovarian cancer, potentially through suppression of ovulation. However, the effect may vary according to the type of contraceptive, duration of use, hormonal composition, and consistency of exposure. In the present study, contraceptive use was categorized relatively broadly as use or non-use. This simple categorization may not adequately capture differences in the duration and type of contraceptive exposure and may therefore have limited the ability to identify an association with histopathological characteristics.

Family history also showed no significant association with the histopathological characteristics of epithelial ovarian cancer in this study. Nevertheless, hereditary susceptibility remains an important consideration in ovarian cancer. Pathogenic variants in BRCA1 and BRCA2 are associated with an increased susceptibility to ovarian cancer and are particularly relevant to certain histopathological subtypes, including high-grade serous carcinoma. The absence of a significant association in the present study may be related to the small number of patients reporting a positive family history. In addition, family history is an indirect indicator of hereditary susceptibility and cannot be considered equivalent

to genetic testing. Therefore, the absence of a significant association should not be interpreted as evidence that hereditary factors are unimportant in ovarian cancer. Overall, the findings of this study indicate that age, parity, contraceptive use, and family history were not significantly associated with the histopathological characteristics of epithelial ovarian cancer in this hospital-based population. The lack of statistically significant associations may reflect the multifactorial nature of epithelial ovarian cancer, differences among histopathological subtypes, and the limited sample size of the study. In addition, the retrospective use of medical records may have limited the availability and detail of reproductive, hormonal, and hereditary information.

CONCLUSIONS AND RECOMMENDATIONS

This study concludes that age, parity, contraceptive use, and family history were not significantly associated with the histopathological characteristics of epithelial ovarian cancer among patients at Tarakan Regional General Hospital, Jakarta. These findings suggest that the histopathological characteristics of epithelial ovarian cancer are multifactorial and may involve complex interactions among reproductive, hormonal, hereditary, clinical, and biological factors. Further multicenter studies involving larger populations and more detailed genetic and reproductive data are recommended to improve the generalizability of the findings and enhance the understanding of factors associated with specific histopathological subtypes of epithelial ovarian cancer.

FURTHER STUDY

This single-center cross-sectional study was limited in establishing causal relationships and obtaining complete information because not all patients could be directly interviewed. Future studies should involve larger multicenter samples and more comprehensive data from interviews and medical records to better evaluate reproductive and hereditary factors associated with epithelial ovarian cancer.

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