

ORIGINAL ARTICLE

Prevalence and Associated Factors of Ovarian Cyst Malignancy: A Cross-sectional Based Study in Surabaya

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ABSTRACT

Introduction: Ovarian cyst is the sac-like formation filled with brownish fluid and sebum in the ovarium. Most ovarian cysts are benign, and the potential to develop malignancy is only 2%. The malignant cyst is considered as cancer type. This study aimed to analyze the prevalence and associated factors of ovarian cyst malignancy. **Methods:** This cross-sectional based study used 84 samples of women with an ovarian cyst in Surabaya. The detection of ovarian cyst is conducted by ultrasound and histopathological examination to determine the level of malignancy. **Results:** From 84 cases, there were 3 cases of ovarian cyst malignancy (3.6%). There was a significant difference in the level of malignancy based on age ($p= 0.000$). The ovarian cyst in patients over 50 years old was more likely to develop into a malignant cyst. The majority of ovarian cysts subtype were bilateral cyst and endometriosis cysts, consist of 31 patients (36.9%) and 22 patient (26.2%) respectively. Analysis for the cyst location, majority of ovarian cysts was located bilaterally consist of 47 patients (56.0%). All patients with malignant cyst were not experience bleeding. There were no significant differences on category of cyst ($p= 0,674$), location of cyst ($p= 0.294$) and the presence of bleeding ($p= 0.541$). **Conclusion:** The prevalence rate of ovarian cyst malignancy was 3.6% with age as a significantly associated factor.

Keywords: Associated factor, Prevalence, Ovarian cyst, Malignancy

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INTRODUCTION

Nowadays, one of the health problems faced by women is the health of reproductive organs. Ovarian cancer is ranked fifth as a cancer-causing death in women (1). The likelihood of a woman developing ovarian cancer in her lifetime is 1:78, while the chance of dying from ovarian cancer is 1: 108. Most ovarian masses are benign, and the potential to develop malignancy is only 2%. Age is a major factor as a risk factor for ovarian malignancy. Adnexal masses often formed during the reproductive age. At this age, these masses are usually caused by functional ovarian cysts, benign ovarian neoplasms, or changes due to infection in the fallopian tubes (2). Ovarian cysts are fluid-filled sacs in the ovaries. An ovarian cyst is a tumour, whether small or large, cystic or solid, benign or malignant. A cyst is a benign tumour that is often found in women in their reproductive years (3). According to Globocan in 2018, 295,414 women worldwide were diagnosed with ovarian cancer

and 4.4% death among them related with ovarian cancer (4). In Indonesia, the incidence rate in 2018 was reported as many as 13,310 women experienced ovarian cysts, and with a mortality rate up to 3.8% (7,842 people died) (5). Ovarian cysts can turn malignant or can be called cancer; besides that, they can also experience torsion or twist, causing pain, bleeding, infection and death in the sufferer. The high mortality rate from ovarian cysts is due to the absence of symptoms or complaints in patients until metastasis occurs, as many as 70% of patients who come to the hospital are usually at an advanced stage (6).

Ovarian cysts are often referred to be the silent killer because many women are late to find out about a cyst when it can be palpable from the outside or enlarged (7). Based on the Indonesian health demographic survey, the incidence of ovarian cysts in Indonesia reaches 37.2%. It often occurs in women aged 20-80 years, at puberty or it is rarely occur in women aged below 20 years (8). Several factors can cause ovarian cysts, such as nulliparous, first birth at the age of over 35 years, women who have a family history of first pregnancy occurred at the age of under 25 years old (9). In most cases, ovarian cysts are benign and can be treated

easily. At premenopausal age, the risk of malignancy of ovarian cysts is 1: 1000 (9), which indicates that ovarian cysts are very rare to develop malignant cyst or cancer. Therefore, this research is required for early detection of ovarian cysts and reduce the risks factor of malignancy.

MATERIALS AND METHODS

This research is an observational analysis with a cross-sectional approach which was conducted at Hajj General Hospital Surabaya for the period 2018-2019. A total of 84 samples were collected during the study.

Transvaginal ultrasound to detect ovarian cyst

The data were collected from ultrasonography (USG) and histopathology examination's results. Ultrasound is the main imaging diagnostic tool for ovarian cysts (11). Transvaginal ultrasound (TVS) is the first-line examination to evaluate adnexal masses. TVS can assess the size, location, structure (cystic, solid, or mixed), vascularization using a power-color doppler and its relationship to surround structures (10). Transvaginal ultrasound (TVS) alone can diagnose adnexal mass malignancies with a specificity of 65-98% and a sensitivity of 48-100% (11). Ovarian morphological abnormalities such as the presence of solid areas or papillary projections of the cyst wall or abnormalities in the volume of solid ovarian tumors can differentiate between benign and malignant diagnoses. The quantitative index or numerical score for the volume and tumor morphology can be used to assess the risk of malignancy. The combined score from volume and morphology of more than 5 can indicate malignancy (12,13)

Histopathological examination for ovarian cyst

Histopathological examination is still considered as the gold standard for definitive diagnosis and therapy of malignant ovarian tumors. Ovarian cyst samples obtained from surgery then made histopathological slides with procedures including tissue fixation with formalin solution and phosphate buffer with a ratio of 1: 9 for 24 hours; tissue processing including dehydration, clearing and impregnation processes; embedding using liquid paraffin at a temperature of 60°C to make frozen and solid paraffin blocks obtained after cooling; cutting paraffin blocks using microtomes with a thickness of 4-6 µm each; hematoxylin-eosin staining (Abcam, Cambridge, UK); mounting, giving entellan liquid on the slide then covered with a cover glass; reading the results is done by making observations under a 400x microscope (Olympus CX23, Tokyo Japan) to see a microscopic characteristic of the cell structure. In H&E staining, the presence of cancer cells and stromal infiltrate will differentiate the stage of ovarian cyst (14). The benign tumor type can be defined as one that has some but not all of the morphological characteristics of malignancy such as stratification of the epithelial cells, clear detachment of cellular clusters from their origin sites, mitotic activity and an intermediate nuclear

abnormalities between those of clearly benign or malignant tumors, also does not have invasion of the adjacent stroma (15).

Data analysis

All data associated with female patients diagnosed with ovarian cysts were used as samples and analyzed by a descriptive statistical test using chi-square and Cramer's V correlation to determine the existence of significant differences in the variables towards the level of malignancy.

RESULTS

The results showed that 3 samples (3.6%) were detected as malignant ovarian cysts from 84 patients with ovarian cysts at Hajj General Hospital in 2018-2019, while the other 81 (96.4) samples were only detected as benign ovarian cysts. Based on age data distribution, the majority of the subject of study were 31-50 years old with a total of 52 patients (61.9%), followed by 21 patients (25.0%) under 30 years old and 11 patients (13.1%) over 50 years old. Based on the distribution of ovarian cyst types, the majority of cyst types were bilateral cysts with 31 patients (36.9%) and endometriosis cysts in 22 patients (26.2%). While, according to the WHO category, most of the types of cysts found were Surface Epithelial Stromal Tumors with 67 patients (79.8%). The majority of ovarian cysts were located bilaterally or on both ovaries were 47 patients (56.0%), 19 patients (22.6%) with ovarian cysts on the right ovary and 18 patients (21.4%) on the left ovary. The number of patients with ovarian cysts who also experienced bleeding was 75 patients (89.3%) while the other patients had no bleeding (10.7%) (Table I).

The analysis results of factors that may have association with the level of malignancy show that only age variable ($\chi^2= 20.646$; $p\text{-value}= 0.000$) had significant effect ($p\text{-value} < 0.05$) on the level of malignancy. It is stated that age variable gives 20 times the chance of having malignancy. while other factors such as cyst category ($\chi^2= 0.798$; $p\text{-value}= 0.674$), cyst location ($\chi^2= 2.449$; $p\text{-value}= 0.249$) and bleeding ($\chi^2= 0.373$; $p\text{-value}= 0.541$) had no significant effect (Table II).

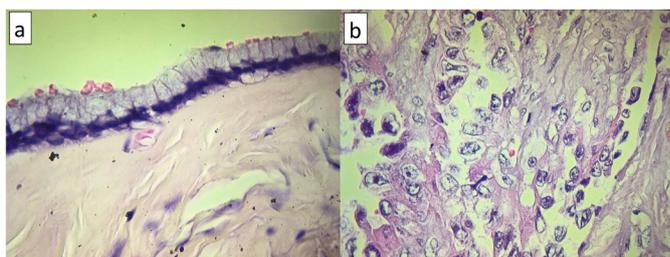


Figure 1 a: Histopathology of benign ovarian tumor with columnar epithelium with basally located hyperchromatic nuclei. **b:** Clear cell carcinoma with predominantly solid pattern and large, highly pleiomorphic nuclei with multinucleated forms. All figure was observed under 400x magnification.

Table I : Data distribution of laboratory test of ovarian cysts

Variables	Category	Number of samples	Percentage (%)	
Malignancy level	Benign	81/84	96.4	
	Malignant	3/84	3.6	
Age	≤ 30 years old	21/84	25.0	
	31-50 years old	52/84	61.9	
	> 50 years old	11/84	13.1	
Type of cyst	Endometriosis cyst	22/84	26.2	
	Mucinous cystadenoma	5/84	6.0	
	Serous cystadenoma	2/84	2.4	
	Seromucinous cystadenoma	2/84	2.4	
	Simple cyst	4/84	4.8	
	Teratoma	4/84	4.8	
	Endometriosis hemoraghic cyst	2/84	2.4	
	Dermoid cyst	2/84	2.4	
	Follicular cyst	1/84	1.2	
	Bilateral cyst	31/84	36.9	
	Adult granulous tumor cell	1/84	1.2	
	Clear cell carcinoma	2/84	2.4	
	High grade serous carcinoma	1/84	1.2	
	Others	5/84	6.0	
	Category of cyst*	Surface Epithelial Stromal Tumors	67/84	79.8
		Sex Cord Stromal Tumors	5/84	6.0
Germ Cell Tumors		12/84	14.3	
Location of cyst	Dextra	19/84	22.6	
	Sinistra	18/84	21.4	
	Bilateral	47/84	56.0	
Bleeding	Yes	9/84	10.7	
	No	75/84	89.3	

* based on WHO category

Table II : Associated factors of ovarian cysts

Variables	Category	Malignancy level		χ ²	p-value
		Malignant (n)	Benign (n)		
Age	≤ 30 years old	0	21	20.646	0.000
	31-50 years old	0	52		
	> 50 years old	3	8		
Category of cyst*	Surface Epithelial Stromal Tumors	3	64	0.798	0.674
	Sex Cord Stromal Tumors	0	5		
	Germ Cell Tumors	0	12		
Location of cyst	Dextra	0	16	2.449	0.294
	Sinistra	0	18		
	Bilateral	3	47		
Bleeding	Yes	0	9	0.373	0.541
	No	3	72		

* based on WHO category

DISCUSSION

The benign tumour often found in women in their reproductive years. At premenopausal age, the risk of malignancy of ovarian cysts is 1: 1000 (9), which indicates that ovarian cyst malignancy is very rare. The number of ovarian cyst cases in Hajj General Hospital Surabaya in 2018-2019 was 84 cases, with malignancy cases was only 3 (3.6%). These data were consistent with a study conducted by Kayastha (16) which found 95 cases of ovarian cysts, 86 cases of benign ovarian cysts (90.5%) and 9 cases (9.5%) found malignancy.

The productive age of women is between 15-49 years (15). At that age, women are prone to ovarian cysts, but the ovarian cysts are very rare to become malignant in their productive age. Ovarian malignancy is generally found in older women or postmenopausal women. About 80% of ovarian cancer cases occur in women over 50 years old (17). Based on the current study of ovarian cyst patients at Hajj General Hospital Surabaya in 2018-2019, the number of malignancies from ovarian cysts was observed in the age group of over 50 years old (Table 2). The data were consistent with the other report, which states that the case of benign ovarian tumours often occur in women aged 20-50 years old and very rarely at pre-puberty (2).

Based on the results of Cramer's correlation statistical analysis, there was a significant correlation between age and ovarian cyst malignancy (the probability value $(p) = 0.000$ ($p < 0.05$). In a study conducted by Nurlailiyani in 2013 (18) also reported a significant correlation between age and ovarian cyst malignancy (p -value= 0.018). A study conducted by Nurlailiyani (2013) showed different results with this study, in which women above 50 years old were more prone to malignant cases. While in this study showed a high prevalence of malignancy was observed among women in productive age (15-49 years old). Whereas in the study by Simamora et al (19) was found no significant relationship between age and the histopathological degree of ovarian cancer (p -value= 0.341). Previous study explained the correlation between age and the incidence of ovarian malignancy, including Johari and Siregar (20) mentioned that increasing age in women might give time for genetic changes of surface epithelial cells in the ovaries.

Ovarian cancer is classified according to the microscopic appearance of the cell structure. Histopathological examination can provide clues for clinical management and prognosis. The macroscopic formation of the biopsy material from ovarian cancer is difficult to distinguish even though the histological types are different (21). Most types of ovarian cysts in this study were endometriosis cysts. In contrast to the research of Simamora et al., (19) which was conducted at Dr. H. Abdul Moeloek Bandar

Lampung, reported that the most types of ovarian cysts were mucinous cystadenoma about 14 of 40 cases (35%) and no malignancy was found in all kinds of ovarian cysts. Meanwhile, in a study by Pudasaini et al., (22) found that the majority of types of ovarian cysts were serous cystadenoma with a frequency of 39 of 102 cases (38.2%).

According to WHO's classification of ovarian tumour types, our study showed that the majority of ovarian cyst malignancies develop from the surface epithelial-stromal tumours with a frequency of 3 cases (100%). In contrast, there were not found malignancy either sex cord-stromal tumours and germ cell tumours. The data from this study were following several works of literature which states that the type of surface epithelial-stromal tumours has the highest percentage and level of malignancy with a percentage of 65-70% and a malignancy rate of 90% of all ovarian tumours. Then it followed by germ cell tumours (15-20 %) with 3-5% malignancy rate, sex cord-stromal tumours (5-10%) with malignancy rate of 2-3%, and metastases (5%) and malignancy rate of 5% (23).

Ovarian cysts can occur in one or both ovaries. According to Lee-Jones (24), approximately 50% of ovarian carcinomas were bilateral, which happened in both ovaries. The likelihood of bilateral involvement in primary ovarian tumours varies depending on the histological subtype. Results from the Surveillance Epidemiology and End Results (SEER) showed that 22,328 women diagnosed with surface epithelial-stromal malignant or borderline ovarian tumours. These women showed bilateral cyst involvement was found in malignant serous ovarian tumour subtypes as much as 57.5%, borderline serous tumours 29.8%, mucinous tumours as much 21.3%, clear cell tumours 13.3%, endometrioid 26.8%, and epithelial tumours 35.6% (25). In some literature, it is stated that the location of ovarian cysts may affect the malignancy of ovarian cysts, but depending on the type of cyst. Pudasaini et al., (22) reported that bilateral cysts were found in 18 of 102 cases (18.6%), and 6 cases were malignant. Similar results also reported by Kayastha (16) showed that 12 of 95 patients had bilateral ovarian cysts with six patient were found to be malignant.

Patient with ovarian cysts can experience torsion or twist, causing pain, bleeding, infection and death in the sufferer. Bleeding from the vagina is one of the symptoms and signs of ovarian cancer, especially in the postmenopausal age. Other symptoms include pain or pressure in the pelvis or lower abdomen, back pain, enlargement of the abdominal area or feeling full, feeling full quickly or having difficulty eating, and changes in bathroom habits (such as frequent urination or constipation) (26). Hamilton et al., (27)

reported that there were seven symptoms associated with ovarian cancer, including the presence of postmenopausal bleeding which had a positive predictive value of 0.5% (0.2% - 0.9%) and an odd ratio= 24 (9.3-64) with a confidence level of 95%, with the conclusion that in 181 cases (85%) women with ovarian cancer in the study usually had at least 1 of 7 reported symptoms.

CONCLUSION

The results showed that the prevalence rate of ovarian cyst malignancy was 3.6%. There were only age variables that had a significant correlation, while other factors such as the type of cyst, location of the cyst, and bleeding had no significant correlation.

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