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Characteristic gynaecology-oncology patients from Obstetrics and Gynaecology Outpatient Clinic Mangusada Regional Hospital Badung referred to Sanglah Hospital from 1st January 2016 – 31st December 2018



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ABSTRACT

Background: Every year, there is an increase in malignancy cases in the world. In women, malignancy is the second most cause of death. Gynecologic malignancy can be found in all women reproductive tract, including cervix, ovary, uterus, vagina and vulva. Most women death from gynecologic malignancy occurred in developing countries, and this is due to lack of access for early detection and treatment. The study aims to report characteristic of patients referred from Obstetrics and Gynaecology Outpatient Clinic Mangusada Hospital, Badung from January 2016 – December 2018.

Results: Total referred case were 451 gynaecology-oncology patients in obstetrics and gynaecology outpatient clinic Mangusada Hospital, Badung-Indonesia. Top three most referred case were cervical cancer,

ovarian cyst with malignancy suspected and ovarian cancer. For Cervical cancer, most of the patients are in group age 41-50 years old (40,3%), in-stadium III (59,2%) and squamous cell type (71,7%). For ovarian cancer, most of the patients are in group age 41-50 years old (45,1%), in-stadium III (59,2%), and epithelial type cell (87,3%). For endometrial cancer, most of the patients are in group age 51-60 years old (53,9%), in-stadium III (46,1%) and adenocarcinoma cell type (100%).

Conclusion: The most common gynaecological referral cases are cervical cancer, suspicious malignant ovarian cysts, and ovarian cancer. All gynaecological cases referred to are suspected or diagnosed as gynaecological malignancies and require the handling of a gynaecology-oncology division and integrated oncology services.

Keywords: referred case, gynaecology oncology, oncology center.

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INTRODUCTION

Malignancy in gynaecology includes all malignancies found in the female reproductive organs, such as the cervix, ovaries, uterus, vagina and vulva. In women, malignancy is the second most common cause of death.

The prevalence, incidence and rate of death of gynaecological malignancies vary with each disease. Malignancy in gynaecology is estimated to reach 20% of total cancer cases in women. In 2012, worldwide there were 14.1 million new cases of malignancy in women and contributed to 8.2 million female deaths worldwide. Meanwhile, in 2014, gynaecological cancer accounted for around 12% (94,990 of 810,320) of all new cancer diagnoses in women in the United States.¹ In the United States around 249,496 women currently live with cervical cancer and 186,138 women live with ovarian cancer. In Indonesia, the overall prevalence of cancer is 4.3/1000 population.² Cervical, ovarian and endometrial cancers rank second, third, and eighth, respectively, most malignancies in women.

The risk of ovarian cancer increases with age. Cervical cancer is strongly associated with HPV infection.³

In the management of cancer cases, it requires management from many experts, including related oncologists, radiologists, nutritionists, and palliatives. In addition, various diagnostic and therapeutic facilities such as colposcopy, radiotherapy, brachytherapy, and chemotherapy are also needed.⁴ Bali Province with a population of around 4,225 million in 2014 currently has only one radiotherapy facility in Sanglah Hospital. Badung Regency with a population of 543,332 people, currently does not have integrated oncology services and still relies on Sanglah Hospital. Sanglah Hospital itself still has a limited number of radiotherapy machines, so surgery and chemotherapy are the first choices for patients with gynaecological malignancies at present.⁵

Survival rates vary in different types of gynaecological malignancies and largely depend on the

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stage at which the malignancy is diagnosed. The five-year survival rates for 2003 to 2009 range from 44% for ovarian cancer to 69% for cervical cancer. However, around 61% of cases of ovarian cancer are diagnosed when it has spread and under these conditions, 5-year survival is only 27%.¹ According to the U.S. Cancer Statistics Working Group, Centers for Disease Control and Prevention, National Cancer Institute in 2015, the prevalence of endometrial cancer reaches 25.1/100,000 (death rate 4.4/100,000), ovarian cancer 11.3/100,000 (death rate 7.4/100,000), vaginal cancer 0.7/100,000 (death rate 0.2/100,000), and vulvar cancer 2.6/100,000 (death rate 0.5/100,000).³

Kematian wanita akibat keganasan lebih banyak terjadi di negara berkembang dibanding dengan negara maju.⁴ Meskipun saat ini didapatkan peningkatan kesadaran tentang pentingnya skrining untuk deteksi dini dan pengobatan kanker ginekologi, penelitian menunjukkan masih banyak perbedaan dalam kualitas perawatan untuk penyakit ini, khususnya sehubungan dengan ras dan status sosial ekonomi. Secara keseluruhan, tampaknya kurangnya akses perawatan standar untuk kanker ginekologi adalah faktor utama penyebab kesenjangan kesehatan di bidang ini. Oleh karena itu diperlukan pemahaman dan data epidemiologis sebagai dasar solusi penatalaksanaan kanker ginekologis di tiap wilayah.⁵

Women's deaths due to malignancy are more common in developing countries than in developed countries.⁴ Although there is now increasing awareness about the importance of screening for early detection and treatment of gynaecological cancers, research shows there are still many differences in the quality of care for this disease, especially concerning race and socioeconomic status. Overall, it seems that the lack of access to standard care for gynaecological cancer is a significant factor causing health disparities in this field. Therefore, understanding and epidemiological data are needed as a

basis for gynaecological cancer management solutions in each region.⁵

This study aimed to provide descriptive data of the oncology gynaecology case which was made a referral from the Mangusada Hospital to The Sanglah Hospital.

METHOD

This study design using cross sectional descriptive model, conducted at the Mangusada Regional Hospital, Badung, Bali-Indonesia from 1st January 2016 - 31st December 2018. Samples were all cases of gynaecology-oncology from the obstetric & gynaecology outpatient clinic in Mangusada Regional Hospital referred to Sanglah Hospital. The data obtained is then collected and processed using the SPSS program version 25.0 for Windows (IBM Corporation, Armonk, NY, USA) and then presented in tabular and narrative form.

RESULT

In the period of 1st January 2016 - 31st December 2018, the total number of gynaecological patient visits at the obstetric and gynaecology clinic of Mangusada Regional Hospital was 3,876 patients with 451 patients being referred. The gynaecological case referred were suspected malignancy or a case that has been diagnosed with gynaecological malignancy.

The number of referral cases is entirely consistent, wherein 2014 there were 232 cases and in 2015 there were 208 cases of gynaecological cancer referrals from the obstetrics and gynaecology clinic of Mangusada Regional Hospital, all of which were referred to Sanglah Hospital. The most commonly referred clinical diagnoses of gynaecology-oncology are cervical cancer, malignant ovarian cysts, and ovarian cancer (Table 1).

Cervical cancer

During the study period 2018, 233 cases of cervical cancer were found in the obstetric and obstetric clinic of Mangusada Regional Hospital, from all gynaecological malignancies, cervical cancer remains the most cancer (51.7%). As shown in the table 2, it is known that cervical cancer patient with the age group of 41-50 have the most significant number (40.3%), with the most stage being stage III (59.2%), and the most histopathological type is squamous (71.7%). Based on Table 3, it was found that the highest incidence of cervical cancer in the age group 41-50 years and the highest stage was found in stage III with a total of 69 patients. In

Tabel 1 Diagnosis of Oncogynecology Cases Referenced from the Mangusada Regional Hospital to Sanglah Hospital

Diagnosis	n=451	%
Cervical cancer	233	51.7
Malignant ovarian cyst	76	16.9
Ovarian cancer	71	15.7
Pre-cancerous cervical lesion	46	10.2
Endometrial cancer	13	2.9
Malignant trophoblast disease	5	1.1
Vulva malignancy	4	0.9
Fallopian tube malignancy	3	0.6

Table 2 Profile of cervical cancer patients in Mangusada Regional Hospital 1st January 2016 - 31st December 2018

Characteristics of cervical cancer	n	%
Age		
< 31 years	7	3.0
31-40 years	34	14.6
41-50 years	94	40.3
years	71	30.5
> 61 years	27	11.6
Stage		
I	24	10.3
II	67	28.8
III	138	59.2
IV	4	1.7
Histological findings		
Adenocarcinoma	61	26.2
Squamous cell carcinoma	167	71.7
Mixed type	5	2.1

Table 3 Cross-tabulation of stadium profile and age of cervical cancer patients in Mangusada Regional Hospital 1st January 2016 - 31st December 2018

Stage \ Age	Age					Total
	< 31 years	31-40 years	41-50 years	51-60 years	> 61 years	
I	3	7	10	4	0	24
II	3	14	29	16	5	67
III	1	15	69	41	12	138
IV	0	0	1	2	1	4
Total	7	36	109	63	18	233

Table 4 Profile of patients with pre-cervical cancer lesions in Mangusada Regional Hospital 1st January 2016 - 31st December 2018

Profile of Cervical Pre Cancer Lesions	n	%
Age		
< 31 years	13	28.3
31-40 years	17	37.0
41-50 years	10	21.7
years	4	8.7
> 61 years	2	4.3
Histology findings		
L-SIL	6	13.0
ASCUS	32	69.6
H-SIL	8	17.4

contrast to cervical cancer, the age of patients with cervical pre-cancerous lesions is found in a younger age range, which is most at the age of 31-40 years. The most commonly found pap smear is ASCUS (69.6%) (Table 4).

Ovarian cancer

Cases of ovarian cancer referral from Mangusada Regional Hospital as much as 15.7%. In addition to ovarian cancer, ovarian cysts suspected of a malignancy (risk of malignancy index > 200) were also immediately referred to Sanglah Hospital in Denpasar due to the unavailability of gynaecology-oncology and frozen section facilities at the Mangusada Regional Hospital. Cases of malignant suspected ovarian cysts were 16.9%. As shown in Table 5, it is known that ovarian cancer patients are most commonly found in the age group of 41-50 (45.1%), with the most stage being stage III (59.2%), and the most histopathological type is epithelial (87.3%). Based on table 6, it was found that the highest incidence of ovarian cancer in the age group of 41-50 years and the highest stage was found in stage III with a total of 21 patients. Similar to ovarian cancer, patients with ovarian cysts suspected of a malignancy (RMI > 200) were also most in the 41-50 years age group with 48.7% (Table 7). This patient was then referred for a laparotomy-frozen section at Sanglah Hospital Denpasar.

Endometrial cancer

Endometrial cancer is the third most gynaecological cancer in our study (9.2%). In our study, most endometrial cancer patients are found in the age group of 51-60 (53.9%), with the most stage being stage III (46.1%), and the most histopathological type is adenocarcinoma (100%) (Table 8). The highest incidence of endometrial cancer in the age group 51-60 years and the highest stage was found in stage III with a total of 6 patients (Table 9).

Age 51-60 is the age group of most endometrial cancer patient in our study. This was also found in a similar study at Sanglah Hospital Denpasar by Budiana et al. with a result of 46.2% in the 51-60 age group.⁶ Other studies at Prof. RSUP dr. R. D. Kandou Manado by Tulumang et al. has a similar findings, where the highest incidence of endometrial cancer in patients over 50 years of age is 66.6%. The incidence of endometrial cancer increases with age. The median age at diagnosis is around 60 years, especially in patients with long-term (unopposed estrogen) exposure, although about 20-25% are found at premenopause.²⁶⁻²⁸

Table 5 Profile of ovarian cancer patients in Mangusada Regional Hospital Period 1st January 2016 - 31st December 2018

Ovarian cancer profile	n	%
Age		
< 31 years	5	7.0
31-40 years	17	23.9
41-50 years	32	45.1
years	11	15.5
> 61 years	6	8.5
Stage		
I	21	29.6
II	5	7.0
III	42	59.2
IV	3	4.2
Histology findings		
Epithelial	62	87.3
Germ Cell	7	9.9
Sex Cord Stromal	2	2.8

Table 6 Cross-tabulation of stadium profile and age of ovarian cancer patients in Mangusada Regional Hospital 1st January 2016 - 31st December 2018

Stage	Age					Total
	< 31 years	31-40 years	41-50 years	51-60 years	>61 years	
I	3	7	10	3	0	23
II	1	1	0	0	0	2
III	1	9	21	8	6	45
IV	0	0	1	0	0	1
Total	5	17	32	11	6	71

Table 7 Profile of suspicious malignant ovarian cyst patients in Mangusada Regional Hospital Period 1st January 2016 - 31st December 2018

Profile of suspicious malignant ovarian cysts	n	%
Age		
< 31 years	4	5.3
31-40 years	15	19.7
41-50 years	37	48.7
51- 60 years	11	14.5
> 61 years	9	11.8
Total	76	100

DISCUSSION

Previous studies conducted at Sanglah Hospital in 2014 showed similar results, namely that cervical cancer was the most severe malignancy in

gynaecology which included 62.2% of all gynaecological cancers, followed by ovarian cancer (24.8%), endometrial cancer (9.2%), vulvar cancer (3.3%) and vaginal cancer (0.5%).

Cervical cancer

Age 41-50 is the age group of the most common age group for cervical cancer in this study, it was also found in a similar study in Sanglah Hospital Denpasar by Prabasari and Budiana in 2012-2013 with 40% results in that age group, as well as in RSUP H Adam Malik Medan in 2011 (58.3%).^{7,8} Other studies at Prof. Dr. dr. R. D. Kandou Manado by Watulingas et al. in the period 2013-2015 also had the same results as the age group broken down into: age 40-44 (14.77%) and age 45-49 (20.48%) with a combined total of 35% for the 41- age group 40 and it also remains the largest age group.⁹ In general, the most cervical cancer patient is those aged >40 years (81.8%) according to research at RSUD dr. Zainoel Abidin Banda Aceh.¹⁰ This is in accordance with the literature which states that the average age of advanced cervical cancer (stage III and IV) is 48 years with a tendency to be diagnosed at ages between 35-55 years and 0.2% are diagnosed under the age of 20 years. This shows that even young women are susceptible to cervical cancer to an advanced stage. This phenomenon is analyzed based on the pathogenesis theory of cervical cancer that is scientifically proven through infection of the human papillomavirus through sexual intercourse at a very young age accompanied by other risk factors such as smoking and multi-partner sexual. Where the process of change from mild, moderate, severe dysplasia to invasive cancer takes time with an extensive range of between 3-17 years. In developing countries such as Indonesia, early detection of cervical cancer is still far from expectations so that patients are often diagnosed at an advanced stage.^{11,12}

Most cervical cancer patients have reached an advanced stage. In this study 59.2% of cases were found in stage III, this is in stark contrast to stage I which was only 10.3%. The role of regular pap smear examination is very necessary for early detection of cervical cancer. In Sanglah Hospital Denpasar and Cipto Mangunkusumo Hospital also found that most patients were in stage III (51% and 41.6%).^{7,10}

The high number of cases referred has reached this advanced stage also illustrates that early detection efforts with primary and secondary prevention are still not optimal, especially in developing countries, education to women of reproductive age has been carried out even programmed by the government and related departments and involving universities, the community and other social

Table 8 Profile of endometrial cancer patients in Mangusada Regional Hospital Period 1st January 2016 - 31st December 2018

Endometrial cancer profile	n	%
Age		
< 31 years	-	-
31-40 years	-	-
41-50 years	2	15.3
51-60 years	7	53.9
> 61 years	4	30.8
Stage		
I	5	38.5
II	2	15.4
III	6	46.1
IV	-	-
Histology findings		
Adenocarcinoma Endometrioid	13	100
Others adenocarcinoma	-	-

Table 9 Cross-tabulation of staging profiles and age of endometrial cancer patients in Mangusada Regional Hospital 1st January 2016 - 31st December 2018

Stage	Age					Total
	<31 years	31-40 years	41-50 years	51-60 years	>61 years	
I	0	0	2	1	1	4
II	0	0	0	0	0	0
III	0	0	0	6	3	9
IV	0	0	0	0	0	0
Total	0	0	2	7	4	13

organizations including women's organizations. This is also likely to be supported by the low knowledge and care of mothers to carry out regular and continuous examinations.¹¹⁻¹⁵

Ovarian cancer

The most ovarian cancer patient from the results of our study are in the age group of 41-50 years. Similar studies at Sanglah Hospital in Denpasar by Dhitayoni et al. shows the same characteristics, the most at the age of 41-50 years (38.4%).¹⁷ Other studies in Medan by Sinaga et al. found that the age group of 36-50 years is the largest group of patients with ovarian cancer.¹⁸ The age of 41-50 years is the age of perimenopause, where this is one of the risk factors that play a role in ovarian cancer, although the effect is not too significant. Evidence is consistent showing that perimenopausal age, nulliparity, early menarche and radiation exposure increase the risk of ovarian cancer.^{16,19,20}

Most ovarian cancer sufferers are found to be in an advanced stage. In this study 59.2% patients were already in stage III. Research at Sanglah Hospital in Denpasar also showed 50.68% of patients were in stage IIIC, 75% of patients were diagnosed in stages III and IV because the initial stadium tends to be asymptomatic and advanced ovarian cancer only causes non-specific symptoms, where the 5-year number survival rate is below 30%. Conversely, if diagnosed in stage I, the 5-years survival rate increases dramatically by 90%.^{21,22}

The most common histology findings are epithelial (87.3%). Other studies also found similar results. The high incidence of epithelial ovarian cancer is analyzed based on the theory of incessant ovulation which considers ovarian cancer to originate from the surface epithelium of the ovary itself. When ovulation occurs, trauma to the ovarian surface epithelium needs to be repaired. During the female reproductive cycle, the process is repeated. During the process the epithelial surface of the ovary is susceptible to DNA damage and transformation. Also, as we get older, the surface of the ovary forms invagination in the cortical stroma. Invagination can cause the surface epithelium to become trapped into the stroma and become an inclusion cyst. As a result of exposure to ovarian hormones, the inclusion cyst can proliferate and if accompanied by DNA damage will lead to malignancy. This is related to other risk factors for ovarian cancer such as the BRCA gene mutation, nulliparity and early menarche.²⁵

Endometrial cancer

Age 51-60 is the age group of most endometrial cancer patient in our study. This was also found in a similar study at Sanglah Hospital Denpasar by Budiana et al. with a result of 46.2% in the 51-60 age group.⁶ Other studies at Prof. dr. R. D. Kandou Hospital by Tulumang et al. has a similar findings, where the highest incidence of endometrial cancer in patients over 50 years of age is 66.6%. The incidence of endometrial cancer increases with age. The median age at diagnosis is around 60 years, especially in patients with long-term (unopposed estrogen) exposure, although about 20-25% are found at premenopause.²³⁻²⁸

In this study 46.1% of cases were found in stage III. In comparison, another study in Sanglah General Hospital in Denpasar also showed that most patients were in stage III (38.5%). Diagnosis of endometrial cancer is often made when examining women with abnormal vaginal bleeding through endometrial biopsy. Approximately 10% of endometrial cancers are associated with complaints of abnormal bleeding during the perimenopause

and post-menopause. In the early stages tend to be asymptomatic so patients are often diagnosed at an advanced stage.^{26,28}

Based on histopathology, the type of cells in endometrial cancer that is most commonly found in the type of adenocarcinoma (100%). Estrogen-dependent endometrial cancer has the highest epidemiology of histological examination in the form of adenocarcinoma with pathogenesis-related to long-term estrogen exposure and begins with endometrial hyperplasia.²⁸

From all gynaecological cases referred, all require gynaecology-oncology treatment. At present in Bali there is only one oncology center, namely in Sanglah Hospital and is a place of reference for gynaecology-oncology cancer patients from Eastern Indonesia. Mangusada Badung Hospital itself is building an oncology center to accommodate some of the referred patients, so it is hoped that services for gynaecology-oncology cancer patients will be more efficient.

CONCLUSION

From the results of this study, it can be concluded that the total number of oncogynecology patients in the obstetric and gynaecology outpatient clinic of Mangusada Regional Hospital referred to Sanglah Hospital in the period of 1st January - 31st December 2018 were 451 patients (12%). The most common gynaecological referral cases are cervical cancer, suspicious ovarian cysts, and ovarian cancer. Cervical cancer is most prevalent in the age group 41-50 years (40.3%), with stage IIIB (59.2%) and histopathological type of epidermoid carcinoma (71.7%). For ovarian cancer, the most common in the age group 41-50 years (45.1%), stage III (59.2%) and histopathological type of epithelial cell carcinoma (87.3%) whereas endometrial cancer was mostly found in the age group 51-60 years (53.9%), stage III (46.1%) and histopathological type of adenocarcinoma (100%). All gynaecological cases referred to are suspected or diagnosed as gynaecological malignancies and require the handling of a gynaecology-oncology division and integrated oncology services.

CONFLICT OF INTEREST

The author declares there is no conflict of interest regarding publication of the study.

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Current study doesn't receive any specific grant from the government or any private sectors.

ETHICAL CONSIDERATION

All data is based on medical record data, thereby ethical clearance is not mandatory.

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