JUXTA: Jurnal Ilmiah Mahasiswa Kedokteran Universitas Airlangga
2023 August, XIV (02)

ORIGINAL ARTICLE

Profile of Endometrial Cancer Patients in Dr. Soetomo General Academic Hospital, Surabaya, Indonesia

Kenny Dion Alim[1], Brahmana Askandar Tjokroprawiro[2], Etty Hary Kusumastuti[3]

[1]Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia.
[2]Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Airlangga/Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.
[3]Department of Anatomical Pathology, Faculty of Medicine, Universitas Airlangga/Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.

ABSTRACT

Introduction: Endometrial cancer is one of the most common cancers that affect the female genitalia. This study aimed to find the profile of endometrial cancer patients in Dr. Soetomo General Academic Hospital, Surabaya, from January 2019 to December 2020.

Methods: Data were collected from medical records of endometrial cancer patients in Dr. Soetomo General Academic Hospital, Surabaya, from January 2019 to December 2020. There were 154 endometrial cancer patients, and 66 met the inclusion and exclusion criteria. Forty-one of those patients also had curettage grades. Data were extracted from the medical records of those patients.

Results: There were 66 samples used in this study. The most common age group of patients was the age group of 51-60 years old (40.91%). The highest parity rate was nullipara (28.79%). The highest body mass index (BMI) group was the normal BMI group (42.42%). The most common type of endometrial cancer was type 1, with endometrioid adenocarcinoma (93.94%). The most common stage of endometrial cancer was stage II (36.36%). The similarity between curettage and post-operative grade was 70.73%. Patients with a history of diabetes mellitus were 6.06%, and patients with a history of hypertension were 12.12%.

Conclusion: Most of the endometrial cancer patients in Dr. Soetomo General Academic Hospital, Surabaya, were women in the age group of 51-60 years old, nullipara, with normal BMI, had type 1 endometrial cancer, and on stage II. Most patients had similar curettage and post-operative grades, and only a minority had diabetes mellitus and hypertension histories.

Highlights:
1. Endometrial cancer is one of the most common cancers that affect the female genitalia.
2. Endometrial cancer patients are mostly women in the age group of 51-60 years old, nullipara, with normal BMI, had type 1 endometrial cancer, and on stage II.

ARTICLE INFO

Article history:

Received 08-11-2022

Accepted 17-07-2023

Available online 10-08-2023

Keywords:
Diabetes mellitus,
Endometrial cancer,
Human & disease,
Hypertension,
Unopposed estrogen.

Cite this as:
Alim KD, Tjokroprawiro BA, Kusumastuti EH. Profile of Endometrial Cancer Patients in Dr. Soetomo General Academic Hospital, Surabaya, Indonesia. *JUXTA J Ilm Mhs Kedokt Univ Airlangga* 2023; 14: 83–88.

* Correspondence: brahmanaaskandar@fk.unair.ac.id

JUXTA: Jurnal Ilmiah Mahasiswa Kedokteran Universitas Airlangga
p-ISSN: 1907-3623; e-ISSN: 2684-9453
DOI: 10.20473/juxta.V14I22023.83-88

Introduction

Endometrial cancer is one of the most common cancers that affect the female genitalia. According to the Global Cancer Observatory (GLOBOCAN), in 2020, endometrial cancer was ranked number 14 as the most common cancer in Indonesia, with 7,773 new cases (2%). In gynecology, endometrial cancer is ranked number 3 as Indonesia's most common gynecological cancer, only behind cervix and ovarian cancer. The number of deaths caused by endometrial cancer in Indonesia in 2020 was 2,626 cases (1.1%). From the world perspective, there were 417,367 new cases of endometrial cancer in 2020, with most of them happening in Asia (40.1%). The number of deaths caused by endometrial cancer worldwide in 2020 was 97,370 cases.[1]

Endometrial cancer can be divided into two types based on histopathological and clinical features, type 1 and type 2. Type 1 endometrial cancer is the most common type, involving 75-90% of all endometrial cancer. Type 1 endometrial cancer is estrogen-dependent. Hence, the pathophysiology of type 1 endometrial cancer is related to unopposed estrogen.[2] Unopposed estrogen is exogenous and endogenous estrogen that is not inhibited by progesterone and can cause mutation of KRAS2 and PTEN genes, leading to endometrial hyperplasia. Endometrial hyperplasia can later develop into endometrial cancer.[3] Endometrioid adenocarcinoma is the most common type of type 1 endometrial cancer. Type 2 endometrial cancer is estrogen-independent, and the pathophysiology is usually started by endometrial atrophy that causes p53 gene mutation, leading to endometrial cancer.[4] There are a few histopathology types of type 2 endometrial cancer, such as serous carcinoma, clear cell carcinoma, small cell carcinoma, malignant mixed Müllerian tumor (MMMT), and undifferentiated carcinoma.[5]

According to the International Federation of Gynecology and Obstetrics (FIGO) 2009, endometrial cancer staging is divided into 4 stages, stage I (IA and IB), stage II, stage III (IIIA, IIIB, IIIC), and stage IV (IVA and IVB).[6] This staging is based on the malignancy and metastasis of the cancer. Stage I endometrial cancer is related to the invasion of the myometrium and the percentage of the invasion to decide stage IA and IB. Stage II endometrial cancer is diagnosed when the tumor has already invaded to cervical stroma. Stage III is diagnosed when the invasion has reached to adnexal, parametrium, vagina, and serous uterine. Stage IV is diagnosed when metastasis has already happened to the bladder, abdominal region, or further.[7]

Type 1 endometrial cancer has histopathological type endometrioid adenocarcinoma. According to the World Health Organization (WHO), this type has grade classification based on epithelial development. Grade 1 tumor has <5% solid non-glandular, nonsquamous growth. Grade 2 has 6-50% solid non-glandular, nonsquamous growth. Grade 3 has >50% solid non-glandular, nonsquamous growth.[6] This grade can be diagnosed with tissue biopsy from curettage and endometrial tissue from operation. The results from these two actions could differ, with the endometrial tissue from operation usually being more accurate than the tissue biopsy from curettage.[8] The implication of the similarity between those two is the sensitivity of the examination as a diagnostic tool. Curettage grades are also vital in deciding the management and therapy of endometrial cancer.[6,8]

The most common symptoms of endometrial cancer are postmenopausal bleeding (about 75% of the patients). For premenopausal women, the usual symptoms are a more frequent menstrual cycle and vaginal bleeding outside the menstrual cycle.[2] Other usual symptoms are abnormal vaginal discharge. For those in the later stage, there are also some other symptoms, such as pelvic pain and abdominal distention.[9]

There are some risk factors for endometrial cancer. The risk factors are divided into 3 groups, reproductive, hormonal, and comorbid. Reproductive factors include nullipara, early menarche, late menopause, and infertility. Hormonal factors are related to an imbalance between estrogen and progesterone levels in the human body that causes unopposed estrogen. These factors include the use of estrogen, selective estrogen receptor modulators (SERM), polycystic ovarian syndrome, and obesity. The comorbid factors include diabetes mellitus and hypertension.[10] It is important to assess these two comorbid factors, especially with the recent increase in patients with hypertension and diabetes mellitus.[11] Other than those risk factors, there is also a risk factor about the patient's age. The majority of endometrial cancer patients are 51-60 years old.[12]

Nullipara is one of the risk factors for endometrial cancer. It is the condition of a woman who has not experienced pregnancy yet. During pregnancy, there is an increase in progesterone levels which suppresses or gives negative feedback to estrogen inside the body, thus preventing unopposed estrogen.[13] Unopposed estrogen can cause the mutation of KRAS2 and PTEN genes, leading to endometrial hyperplasia. Endometrial hyperplasia can develop into endometrial cancer.[2,13]

Obesity is also one of the risk factors for endometrial cancer. People with obesity have more visceral fat than normal people. This visceral fat, such as adipocytes and preadipocytes, are the sources of aromatase enzymes.[14] The function of aromatase enzymes is to change androgen to estrogen.[15] This can cause excessive amounts of estrogen in the body and lead to unopposed estrogen in a person with obesity and then cause mutation of KRAS2 and PTEN genes, thus causing endometrial cancer.[2,14] Obesity in someone can be determined by calculating their body mass index (BMI). BMI are statistical index to estimate the body fat of someone using their body weight and body height. According to WHO classification, there are 4 categories of BMI, underweight (BMI <18.5), normal weight (BMI 18.5-24.9), overweight (BMI 24.9-29.9), and obesity (BMI ≥30).[16]

The most common tests for diagnosing endometrial cancer are transvaginal ultrasonography and endometrial biopsy.[17] Endometrial biopsy can be performed most often by dilation/curettage methods, but lately, there have been newer Pipelle methods that can be used to help diagnose endometrial cancer as an alternative.[8] Physical

examination still needs to be performed for initial diagnosis by looking for other sources of abnormal bleeding and feeling the uterus and adnexa part if there is probably a mass or tumor. There are no specific laboratory tests, only some general tests, such as a complete blood count and prothrombin time for patients who have vaginal bleeding. Papanicolaou smear examination can sometimes be used to diagnose endometrial cancer. Saline infusion sonohysterography can be considered as a diagnosis for endometrial cancer if transvaginal ultrasonography and endometrial biopsy are not possible.[18] Other diagnosis methods are hysteroscopy to examine vaginal bleeding and also other imaging examination such as magnetic resonance imaging (MRI) to examine endometrial thickness.[19]

There are several treatments for endometrial cancer patients. The most common treatment for early stages is surgery.[20] The surgeries that can be performed are bilateral salpingo-oophorectomy, total hysterectomy, radical hysterectomy, and lymph node dissection, depending on the severity of endometrial cancer.[21] Endometrial cancer can also be treated with radiation therapy.[19,21] Radiation therapy is therapy for endometrial cancer patients by using high-energy X-rays or other types of radiation to kill cancer cells. There are two types of radiation therapy, external and internal. External radiation therapy uses a machine outside the body that emits radiation to the part of the body affected by the cancer. Meanwhile, internal radiation therapy uses a radioactive substance contained in needles, radioactive seeds, cables, and catheters that are placed directly near the cancer cells. Other therapies included chemotherapy and hormonal therapy.[19]

Endometrial cancer is one of the diseases that cannot be looked upon. The number shows that this cancer is one of the most common gynecological cancers in women, and the number of cases is high each year. Endometrial cancer also has several risk factors, meaning that endometrial cancer can be prevented if these risk factors can be avoided. Based on the known risk factors, the number of cases, and the fact that there has been no research on the profile of endometrial cancer patients in Dr. Soetomo General Academic Hospital, Surabaya, recently, this study aimed to provide information about endometrial cancer profile and as a strategy to reduce the number of endometrial cancer cases.

Methods

This was a descriptive retrospective study. The samples were taken from medical records of endometrial cancer patients in the Medical Records Center and the Department of Anatomical Pathology Dr. Soetomo General Academic Hospital, Surabaya, from January 2019 to December 2020. The ethical clearance had been approved by the Ethical Committee of Dr. Soetomo General Academic Hospital, Surabaya. The variables were patients' age, parity, BMI, histopathological type, stage, curettage grade, post-operative grade, history of diabetes mellitus, and history of hypertension. All the variables, except endometrial cancer grade, were taken from the medical records of the patients. Endometrial grade variables were taken from the Department of Anatomical Pathology in the form of a digital database and matched with medical records numbers to get the curettage grade and post-operative grade of each patient. All of the data were arranged in worksheets as digital data. All information about the patient's identity and personal information was concealed to meet the confidential principles.

The number of medical records of endometrial cancer patients taken from January 2019 to December 2020 was 154. These 154 patients were inpatients and outpatients who had been treated at Dr. Soetomo General Academic Hospital, Surabaya, but some of them did not have the data about the required variables in this study and only 66 patients fit the inclusion criteria. The inclusion criteria were all the endometrial cancer patients in Dr. Soetomo General Academic Hospital, Surabaya, from January 2019-December 2020 that had all the data of the variables needed (had at least post-operative grade). Meanwhile, the exclusion criteria were patients without complete data about the required variables or the data were invalid. From 66 patients that fit the inclusion criteria, 41 patients had both the curettage grade and post-operative grade of endometrial cancer.

Results

Sixty-six samples were used in this study. As seen from Table 1, the most common age group of patients was the age group of 51-60 years old with 27 from 66 patients (40.91%), followed by the age group of 41-50 years old with 21 from 66 patients (31.82%), age group >60 years old with 12 from 66 patients (18.18%), and lastly age group ≤40 years old with 6 from 66 patients (9.09%). The highest parity rate was nullipara or parity 0 with 19 from 66 patients (28.79%), followed by parity 2 with 15 from 66 patients (22.73%), parity 1 with 13 from 66 patients (19.70%), parity 3 with 13 from 66 patients (19.70%), and parity >3 with 6 from 66 patients (9.09%).

The highest BMI group was the normal BMI group with 28 from 66 patients (42.42%), followed by the obesity group with 19 from 66 patients (28.81%), the overweight group with 16 from 66 patients (24.24%), and lastly the underweight group with 3 from 66 patients (4.54%). The most common type of endometrial cancer was type 1, which was endometrioid adenocarcinoma in 62 of 66 patients (93.94%). Type 2 was found in 4 from 66 patients (6.06%), which consisted of serous carcinoma with 1 from 66 patients (1.51%), clear cell carcinoma with 1 from 66 patients (1.51%), mixed cell carcinoma with 1 from 66 patients (1.51%), and lastly carcinosarcoma with 1 from 66 patients (1.51%).

The majority stage of endometrial cancer in this study was stage II with 24 from 66 patients (36.36%), followed by stage III with 20 from 66 patients (30.30%), stage I with 14 from 66 patients (21.22%), and lastly stage IV with the least number of patients from the other endometrial cancer stages with 8 from 66 patients (12.12%). Of those 66 endometrial cancer patients, the number of patients with a history of diabetes mellitus was 4 from 66 patients (6.06%).

Meanwhile, endometrial cancer patients with a history of hypertension were 8 from 66 patients (12.12%).

Table 1. Results of endometrial cancer patients' profile

Variable	N = 66	%
Age		
≤40 years old	6	9.09
41-50 years old	21	31.82
51-60 years old	27	40.91
>60 years old	12	18.18
Parity		
0	19	28.79
1	13	19.70
2	15	22.73
3	13	19.70
>3	6	9.09
BMI		
Underweight (BMI <18.5)	3	4.54
Normal weight (BMI 18.5-24.9)	28	42.42
Overweight (BMI 24.9-29.9)	16	24.24
Obesity (BMI ≥30)	19	28.79
Histopathological Type		
Type 1	62	93.94
Type 2	4	6.06
Stage		
I	14	21.22
II	24	36.36
III	20	30.30
IV	8	12.12
History of Disease		
Diabetes Mellitus	4	6.06
Hypertension	8	12.12
Curettage Grade		
1	15	36.59
2	17	41.46
3	9	21.95
Post Operative Grade		
1	8	27.59
2	12	41.38
3	9	31.03

Source: Research data, processed

There were 66 patients with at least one data about endometrial cancer grades in their medical records. From 66 patients, 41 patients had both data of curettage grade and post-operative grade. The majority of curettage grades were grade 2, with 17 from 41 patients. Twelve of 17 patients had the same post-operative grade and 5 patients had different post-operative grade, either grade 1 or 3. Therefore, the similarity in grade 2 of the curettage grade was 70.59%. Of the curettage grade of 15 patients in grade 1, 8 patients had the same post-operative grade, hence the similarity was 53.33%. The curettage grade of 9 patients in grade 3, with all of them having the same post-operative grade, had a similarity of 100%.

Discussion

The majority of the age group in this study was 51-60 years old (40.91%). These results are similar to a previous study by Dewi and Budiana (2017), stating that the most common age group was 51-60 years old (46.2%).[22] In another study, Sofyan (2020) also stated that the age group of 51-60 was the most susceptible to endometrial cancer.[12] This is also similar to another study that stated endometrial cancer patients were in the postmenopausal period, as the average menopausal age was 53 years old.[23] The mechanism around endometrial cancer patient's age is related to the accumulation of unopposed estrogen over the year.[22]

Parity is one of the risk factors for endometrial cancer. In this study, the majority of parity was parity 0 or nullipara (28.79%). These results are similar to the previous study by Mirhalina (2020), which also had nullipara as the majority of parity in endometrial cancer patients (51.61%).[24] Another study by Jayawickcrama and Abeysena (2019) showed a different result with the majority of parity in endometrial cancer patients being multipara (57.8%).[25] Different sample sizes and research fields can cause a percentage difference. The theory also fits with nullipara as a risk factor for endometrial cancer.[10] During pregnancy, there is an increase in progesterone levels which suppresses or gives negative feedback to estrogen inside the body, thus preventing unopposed estrogen.[13] Unopposed estrogen can cause the mutation of KRAS2 and PTEN genes which can cause endometrial hyperplasia and can lead to endometrial cancer.[10,26] Thus, women who already experience pregnancy are more unlikely to suffer from endometrial cancer than nullipara women or women who have not experienced pregnancy yet.[10]

Obesity is another risk factor for endometrial cancer. The best way to determine obesity is by calculating the BMI. There are 4 categories of BMI according to WHO classification, underweight (BMI <18.5), normal weight (BMI 18.5-24.9), overweight (BMI 24.9-29.9), and obesity (BMI ≥30).[16] In this study, the majority of BMI is the normal weight (42.42%). These results differ from another study by Christian in Yuana (2019), stating that the most common BMI in endometrial cancer patients was the obesity and overweight group (68.8%).[26] A different result showed in a study by Siti, *et al*. (2022), with normal weight as the majority of BMI in endometrial cancer patients (41%).[27] The theory about obesity as a risk factor for endometrial cancer also differs from the results of this study.[10] People with obesity have more visceral fat than normal people. This visceral fat, such as adipocytes and preadipocytes, are the sources of aromatase enzymes.[14] The function of aromatase enzymes is to change androgen to estrogen. The excess amount of estrogen that is produced by these enzymes can cause unopposed estrogen in a person with obesity and cause mutation of KRAS2 and PTEN genes, thus causing endometrial hyperplasia. Endometrial hyperplasia can develop into endometrial cancer.[13,28]

The histopathological type of endometrial cancer in this study was dominated by type 1 endometrial cancer (93.94%), while only 6.06% of the patients had type 2 endometrial cancer. These results are linear with another previous study by Helmanda and Yuliawati (2019), stating that the majority of endometrial cancers were type 1 (75%).[28] Casey, *et al*. (2019) also stated that type 1 endometrial cancer, also known as endometrioid

adenocarcinoma, was the most common type, covering about 80-90% of all endometrial cancer.[3,29]

Endometrial cancer staging depends on when the patients are diagnosed with endometrial cancer. In this study, most patients were on stage II (36.36%). The result is similar to another study from Christian in Yuana (2019), stating that most of the patients were also on stage II (37.5%).[26] Another study by Dewi and Budiana (2017) showed different results, with stage III (38.5%) as the majority of endometrial cancer stage.[22] Different sample sizes and research fields can cause differences in these studies, but they also can be caused by the different quality of diagnostic approaches in every hospital. The differences in percentage can also be affected by patients' awareness of their condition regarding the cancer.[22,26]

The similarity between curettage grade and post-operative grade in this study was 70.73%. This result is similar to another study by Lago, *et al*. (2018), stating that the similarity between curettage grade and post-operative grade was 76.58%.[30] The implication of the similarity between these two grades is the sensitivity of the tissue examination from curettage as a diagnostic approach. The patient's curettage grade does not always show a definitive grade, which can be compared to the patient's tissue taken from the surgery procedure (post-operative grade).[8] The greater the percentage, it shows the quality of the examination. In this case, the percentage showed that Dr. Soetomo General Academic Hospital, Surabaya, had a good quality curettage diagnosis showed by a high percentage of similarity between curettage grade and post-operative grade.[8]

The minority of endometrial cancer in this study had diabetes mellitus (6.06%) and hypertension (12.12%). A previous study by Dewi and Budiana (2017) showed similar results, only a minority of the patients had diabetes mellitus (11.5%) and hypertension (11.5%).[22] Another study by Jayawickcrama and Abeysena (2019) showed the same results with a higher percentage, 21.7% of patients had diabetes mellitus and 30.1% had hypertension longer than 5 years.[25] Diabetes mellitus is a type of metabolic syndrome involving defective insulin secretion, insulin action, or both.[31] Diabetes mellitus has increased expression of IGF1 and insulin that can cause excessive endometrial proliferation.[14] Meanwhile, the mechanism of hypertension to endometrial cancer is unknown but most likely related to the mechanism of apoptosis.[32] These results show that diabetes mellitus and hypertension are risk factors for endometrial cancer but are probably not as impactful as the other risk factors.[32]

Strength and Limitations

This study discussed the newest profiles, all related risk factors of endometrial cancer patients, and some risk factors that have not been discussed in other research for some period of time.

The limitation of this study was the lack of data in patients' medical records, further hindering the process of collecting. It also caused the reduction of the samples of more than half of all the endometrial cancer patients in Dr. Soetomo General Academic Hospital, Surabaya, over the period of time.

Conclusion

This study showed that there were some groups of women in certain age groups, parity, BMI, diabetes mellitus, and hypertension history who were more at risk of having endometrial cancer. Still, there were some biases that could happen in this study considering the close location and small sample sizes. Further research about endometrial cancer with broader locations and samples is needed to produce more accurate results.

Acknowledgments

Special thanks to the Medical Records Department and the Department of Anatomical Pathology Dr. Soetomo General Academic Hospital, Surabaya, for their assistance in this study.

Conflict of Interest

The authors declared there is no conflict of interest.

Funding

This study did not receive any funding.

Ethical Clearance

This study had received ethical clearance from the Ethical Committee of Dr. Soetomo General Academic Hospital, Surabaya, (no. 0732/LOE/301.4.2/XII/2021) on 22 December 2021.

Authors' Contributions

Designed the study and drafted the manuscript: KDA. Collected data and performed background literature review: KDA. Performed statistical analysis: KDA. Supervised results and discussion: KDA, BAT, and EHK. All authors reviewed and approved the final version of the manuscript.

References

1. Sung H, Ferlay J, Siegel RL, *et al*. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* 2021; 71: 209–249. [Journal]
2. Suarez AA, Felix AS, Cohn DE. Bokhman Redux: Endometrial Cancer 'Types' in the 21st Century. *Gynecol Oncology* 2017; 144: 243–249. [ScienceDirect]
3. Casey MJ, Crotzer D. *Endometrial Cancer*. StatPearls Publishing, 2019. [NCBI]
4. Zhou Q, Singh S, Tina S, *et al*. The Pathways in Endometrial Carcinogenesis and an Overview of its Histology, Grade and Stage. *Ann Clin Lab Res*; 06. Epub ahead of print 1 January 2018. [Journal]
5. World Health Organization (WHO). *Female Genital Tumours*. Geneva, https://publications.iarc.fr/592 (2020). [Book]
6. Soslow RA, Tornos C, Park KJ, *et al*. Endometrial Carcinoma Diagnosis: Use of FIGO Grading and Genomic Subcategories in Clinical Practice: Recommendations of the International Society of

Gynecological Pathologists. *Int J Gynecol Pathol*
7. McCluggage WG. Pathologic Staging of Endometrial Carcinomas: Selected Areas of Difficulty. *Adv Anat Pathol* 2018; 25: 71–84. [Journal]
8. Inal ZO, Inal HA, Kucukosmanoglu I, *et al*. Assessment of Endometrial Sampling and Histopathological Results: Analysis of 4,247 Cases. *Eurasian J Med* 2017; 49: 44–47. [NCBI]
9. Jones ER, O'Flynn H, Njoku K, *et al*. Detecting Endometrial Cancer. *Obstet Gynaecol* 2021; 23: 103–112. [ResearchGate]
10. Gupta D. Clinical Behavior and Treatment of Endometrial Cancer. *Adv Exp Med Biol* 2017; 943: 47–74. [Book]
11. Dewanto RR, Munir RS, Djuari L. Manajemen Penderita Hipertensi di Puskesmas Pacar Keling 18-31 Mei 2015. *JUXTA J Ilm Mhs Kedokt Univ Airlangga* 2017; 9: 54–59. [Journal]
12. Sofyan N, Sudiana IK, Askandar B. Profile of Endometrial Cancer Patients in the Third Referral Hospital in Surabaya based on Known Risk Factors. *Biomol Heal Sci J* 2020; 3: 67–70. [Journal]
13. Sponholtz TR, Palmer JR, Rosenberg L, *et al*. Reproductive Factors and Incidence of Endometrial Cancer in U.S. Black Women. *Cancer Causes Control* 2017; 28: 579–588. [NCBI]
14. Yang X, Wang J. The Role of Metabolic Syndrome in Endometrial Cancer: A Review. *Front Oncol* 2019; 9: 744. [Journal]
15. Sood A, Lang DK, Kaur R, *et al*. Relevance of Aromatase Inhibitors in Breast Cancer Treatment. *Curr Top Med Chem* 2021; 21: 1319–1336. [PubMed]
16. Weir CB, Jan A. BMI Classification Percentile and Cut Off Points. Treasure Island (FL), 2023. [ResearchGate]
17. Passarello K, Kurian S, Villanueva V. Endometrial Cancer: An Overview of Pathophysiology, Management, and Care. *Semin Oncol Nurs* 2019; 35: 157–165. [ScienceDirect]
18. Kumar K, Pajai S, Baidya GR, *et al*. Utility of Saline Infusion Sonohysterography in Gynecology: A Review Article. *Cureus* 2023; 15: e35424. [NCBI]
19. Oaknin A, Bosse TJ, Creutzberg CL, *et al*. Endometrial Cancer: ESMO Clinical Practice Guideline for Diagnosis, Treatment and Follow-Up. *Annals of Oncology : Official Journal of the European Society for Medical Oncology* 2022; 33: 860–877. [PubMed]
20. Rahestyningtyas E, Mulawardhana P, Lesmana T. Abdominal Skin Metastasis in Endometrial Cancer. *Maj Obstet Ginekol* 2019; 27: 84–89. [Journal]

[NCBI] 2019; 38 Suppl 1: S64–S74.
21. Tung H-J, Huang H-J, Lai C-H. Adjuvant and Post-Surgical Treatment in Endometrial Cancer. *Best Pract Res Clin Obstet Gynaecol* 2022; 78: 52–63. [ScienceDirect]
22. Paramitha Dewi PP, Budiana ING. Profil Pasien Kanker Endometrium di RSUP Sanglah Denpasar Periode Agustus 2012 – Juli 2014. *E-Jurnal Med Udayana* 2017; 6: 1–7. [Journal]
23. Peacock K, Ketvertis KM, Doerr C. Menopause (Nursing). Treasure Island (FL), 2023. [Book]
24. Mirhalina S. Jenis dan Faktor Risiko Kanker Endometrium di Rumah Sakit dr Pirngadi Kota Medan Tahun 2015-2018. *J Pandu Husada* 2020; 1: 184–188. [Journal]
25. Jayawickcrama WIU, Abeysena C. Risk Factors for Endometrial Carcinoma among Postmenopausal Women in Sri Lanka: A Case Control Study. *BMC Public Health* 2019; 19: 1387. [BMC Public Health]
26. Yuana E, Silitonga HA, Fauzi TM. Hubungan Indeks Massa Tubuh dan Jumlah Paritas dengan Tipe-Tipe Kanker Endometrium. *J Kedokt Methodist* 2021; 14: 1–11. [Journal]
27. Putri SSAKGNAWDSHN. Profil Penderita Kanker Endometrium di RSUP Dr. Hasan Sadikin Bandung Periode Tahun 2017-2020. *Indones J Obstet Gynecol Sci* 2022; 234–243. [Journal]
28. Helmanda YYS. Factors Related to Type of Endometrial Cancer in RSUP Dr. M. Djamil Padang. *Indones J Obstet Gynecol Sci* 2019; 157–165. [Journal]
29. Rosdiana YE, Sandhika W. The Difference of PGE2 and COX-2 Expressions in Various Histological Grading of Endometrial Endometrioid Carcinoma. *Maj Obstet Ginekol* 2018; 25: 1–5. [Journal]
30. Lago V, Martín B, Ballesteros E, *et al*. Tumor Grade Correlation between Preoperative Biopsy and Final Surgical Specimen in Endometrial Cancer: The Use of Different Diagnostic Methods and Analysis of Associated Factors. *Int J Gynecol Cancer* 2018; 28: 1258–1263. [ResearchGate]
31. Adha AZNA, I'tishom R, Rizaldi F, *et al*. Profile of Diabetes Mellitus in Benign Protate Hyperplation's Patients with Urinary Retention in Dr. Soetomo 2016. *JUXTA J Ilm Mhs Kedokt Univ Airlangga* 2019; 10: 71–74. [Journal]
32. Aune D, Sen A, Vatten LJ. Hypertension and the Risk of Endometrial Cancer: A Systematic Review and Meta-Analysis of Case-Control and Cohort Studies. *Sci Rep* 2017; 7: 44808. [NCBI]