CLINICAL CHARACTERISTICS AND TREATMENT OUTCOMES OF PATIENTS WITH ENDOMETRIAL CANCER IN KENYATTA NATIONAL HOSPITAL, 2012-2018

PRINCIPAL INVESTIGATOR

DR. YONI BIKO

H58/6973/2017, MBChB

DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY,

THE UNIVERSITY OF NAIROBI

A dissertation submitted in partial fulfillment of the requirements for the award of the degree of Master of Medicine in Obstetrics and Gynecology, University of Nairobi.

December 2020

DECLARATION

I declare that this thesis is my original work and that it has not been submitted, in whole or in part, in any previous application for a degree or honorary publication. Except where stated otherwise, by reference or acknowledgment, the work presented is entirely my own.

PRINCIPLE INVESTIGATOR

Dr. Yoni Steve Biko

Signature ……  ……Date ……16/12/2020…….

SUPERVISORS

Dr. Rose J. Kosgei,

MBChB; MMed; MSc

Consultant Obstetrician Gynaecologist KNH

Senior Lecturer, Department of Obstetrics and Gynaecology

University of Nairobi.

Signature  Date 17-12-2020

Dr. Jacqueline Chesang,

MBChB; MMed; PhD

Consultant, Obstetrician Gynaecologist

Lecturer, School of Public Health

University of Nairobi

Signature:  Date:17 – 12 - 2020

CERTIFICATE OF AUTHENTICITY AND DEPARTMENTAL APPROVAL

This is to certify that this dissertation is the original work of Dr. YONI STEVE BIKO, registration number H58/6973/2017, who is a Master of Medicine (MMed) student in the department of Obstetrics and Gynecology (Obs & Gyn), School of Medicine, College of Health Sciences, University of Nairobi (UON). The research was carried out in the department of Obstetrics and Gynaecology, University of Nairobi and Kenyatta National Hospital (KNH). It was carried out under the supervision of DR. ROSE KOSGEI and DR JACQUELINE CHESANG. It has not been presented in any other university for award of a degree or diploma.

Signature. 

Professor Eunice Cheserem,

Associate Professor of Obstetrics and Gynaecology,

Consultant Obstetrics and Gynaecology,

Chairman, Department of Obstetrics and Gynaecology,

University of Nairobi.

DEDICATION

This work is dedicated to Chepchirchir Tanui, whose support and sacrifice has proven vital all through the process of coming up with this dissertation. To my mother, Margaret Moro and sister Marciana Ajwang who have encouraged me to completion.

ACKNOWLEDGEMENT

My supervisors, Dr Rose J. Kosgei and Dr Jacqueline Chesang who have provided guidance support and patience through this process.

The staff at the Department of Medical Records, Kenyatta National Hospital who facilitated my data collection.

The Department of Obstetrics and Gynaecology, University of Nairobi.

My research assistants, statisticians and analysts who provided vital input in the study.

LIST OF ABBREVIATIONS

BMI – Body mass index

BSO - Bilateral salpingo-oophorectomy

EBRT – External beam radiotherapy

EMC – Endometrial cancer

HICs – High-income countries

KNH – Kenyatta National Hospital

LMICs – Low and middle-income countries

RT – Radiotherapy

RCT – Randomized controlled trial

TAH - Total abdominal hysterectomy

VBT – Vaginal brachytherapy

OPERATIONAL DEFINITION

Endometrial cancer: refers to malignant tumours affecting the endometrium

Oncology Center: any healthcare setting that is primarily focused on managing cancer patients

Survival rate: describes the percentage of people still alive at the end of a given period of time since diagnosis

Staging: refers to the categorization of endometrial cancer based on the extent of the disease at the time of diagnosis.

Age-standardized incidence rate: describes the weights given by the number of individuals in each age group per 100,000 in the standard population

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ABSTRACT

Background: Globally, endometrial cancer (EMC) is among the commonest gynecological malignancies occurring in women. The global age-standardized incidence rate of endometrial cancers is 8.2 per 100,000 while the death rate is 1.8 per 100,000. Although lower incidences of EMC are reported in India and African countries compared to Europe and North America, this has been partly attributed to under surveillance. In Kenya, there is lack of data on the characteristics of patients diagnosed with EMC, their management, and outcomes.

Aim of the Study: To evaluate the clinical characteristics and treatment outcomes of patients managed for EMC at Kenyatta National Hospital (KNH), 2012 -2018.

Methodology: A descriptive cohort study was conducted in the medical records department at Kenyatta National Hospital using data from patients' files using a pre-approved data collection tool. The hospital files of all women with histologically confirmed endometrial cancer, managed at KNH between 2012 and 2018 were reviewed and data on demographic characteristics, clinical presentation, treatment modalities, treatment outcomes, and duration of survival collected. Where possible, participants were contacted by telephone to obtain missing data. Version 24 of the statistical package for social scientists' software was used to analyse data. Summary statistics were computed and presented as frequencies, percentages, and means with standard deviation. The Kaplan Meier analysis method was used to evaluate the two-year and five-year cumulative survival rates.

Results: Data of 68 women was reviewed. The mean age of participants was 63 (range 37-87) years. A majority were unemployed (56.9%), had primary education (54.5%), married (61.5%)and resided in Nairobi County (38.2%). The predominant comorbidities were chronic hypertension (57.4%) and diabetes (25%). Vaginal bleeding after menopause was the commonest presenting symptom (80.9%), followed by abdominal pain (38.2%) and vaginal discharge (26.5%). Endometroid adenocarcinoma (68.2%), mostly at grade 2 (55.9%) and stage I (26.7%), was the commonest histological subtype. A majority underwent surgery (96.7%), predominantly the total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO) (83.1%). The remission, recurrence, and mortality rate among the participants were 66.7%, 30.6%, and 28.4%, respectively. The survival rates were 75.8% at two years and 72.8% at five years.

Conclusion: Women with endometrial cancer seen at KNH have a good prognosis. Endometrial adenocarcinoma is the commonest histological subtype, with a majority presenting with postmenopausal vaginal bleeding and or discharge. TAH-BSO is the commonest treatment.

INTRODUCTION

Endometrial cancer (EMC), also known as uterine cancer, is a type of cancer affecting the endometrium, the inner lining of the uterus (1). It results from the out-of-control growth of the endometrial cells. Depending on the predisposing factor, which is often excessive or unopposed estrogen exposure, the endometrial cells undergo damage to their nuclear DNA (atypia). Since this DNA controls the cell cycle, the endometrial cells lose their normal ability to grow, replicate and die (2). With changes in the nuclear DNA, cells have undergone malignant transformation leading to cells growing abnormally in both their structures and numbers.

Statistics indicate an unequal distribution of EMC with a greater disease burden in high-income countries (HICs) than low and middle-income countries (LMICs). This is partly thought to be due to higher surveillance and reporting in (HICs). Another major reason is thought to be an increase in the “cancer-causing” lifestyle, which is sedentary with poor diet and consumption of alcohol and smoking. These factors are on the rise in (LMICs) which is reflected in rising numbers of EMC cases. Risk factors associated with the development of EMC are associated with estrogen excess. Early menarche, late menopause, nulliparity, use of estrogen-only contraceptives and hormone replacement therapy, and obesity are the highest-ranking factors. There is also an association with other malignancies like colon cancer and syndromes such as LYNCH syndrome. Family history of malignancy and specifically EMC is also a risk factor. Comorbidities, specifically Diabetes, and hypertension are commonly associated with EMC since the lifestyle-related factors are similar.

There are two types of EMC recognized. Type I (85%) is estrogen-dependent, more common in older (>60 years) women, and has better survival rates with treatment. Type II (15%) not estrogen-dependent, occurring in younger, thinner women, and is more aggressive.

The mainstay of treatment is surgery, variations of TAH/BSO depending upon type and stage of malignancy as well as patient profile. There is a role for chemotherapy and radiotherapy in the treatment of the disease. Progestin based hormone therapy is used both in primary treatment and upon disease recurrence. Treatment outcomes are generally good with 5-year survival rates averaging 85% but this varies based on various patient factors.

Globally the average age of EMC patients is 63 years and currently, no standardized screening protocol exists. Lack of protocol is suggested to be due to a relatively low incidence rate, older patient profile, and good treatment outcomes. This does not negate the fact that uterine cancer (EMC) is among the commonest gynecological malignancies globally. In the USA, according to the Center for Disease Control and Prevention statistics, endometrial cancer is the commonest gynaecological malignancy with an incidence of 26.82 cases per 100,000 women (3).Consequently, more attention is required to understand the disease and patient profile so that clinicians and patients can take measures to prevent the disease in younger women.

LITERATURE REVIEW

Introduction

The literature review offers a description of previous research work done on endometrial cancer, related management approaches, and patient outcomes. The discussion of key concepts related to EMC in this review will use sections. The first section will offer the epidemiology of EMC, focusing on the prevalence and incidence rates. The second section will look at both the classification and staging of EMC. The third section will examine the risk factors of EMC, which will be followed by its pathophysiology. The approaches to assessing and diagnosing EMC and the management approaches available in healthcare settings will also be discussed. The review will also examine the outcomes of EMC, specifically focusing on prognosis, survival rates, and complications. At the end, we provide the conceptual framework guiding this research study, the summary, and the research gap.

Epidemiology of Endometrial Cancer

Globally, the age-standardized incidence rate of EMC has been reported to be 8.2 per 100,000 while the death rate is 1.8 per 100,000 (4). Rates of EMC vary between regions. North America and Europe report incidence rates of more than 10 per 100,000 which is greater than the average global incidence(5). There also exist differences in racial distribution of the disease with white women showing a larger incidence rate. This was demonstrated in a study in America that also showed a paradoxically lower 5-year survival rate in black women (64%) compared to 84% in white women who had a larger disease burden(6). Henley et al reported that the incidence rate of EMC in America increased by 0.7% every year between 1999 and 2015 and the mortality rate

increased by 1.1% yearly between 1999 and 2016(7). In support, Siegel et al. has indicated that 4.6 per 100,000 women die due to EMC (8). Similar results have been reported in Europe where four women per 100,000 die of EMC (5).

In Africa, however, the incidence rate is relatively lower than in the HICs. Alshahrani et al found an age-standardized rate of 4.1 per 100,000 in Egypt(9). In support, Joseph et al indicated that only 10.1% of the 1,178 patients examined in a Nigerian teaching hospital had EMC(10). Similarly, findings by Macharia et al did not qualify EMC as among the top five cancers in Kenyatta National Hospital (KNH).(11) India is among the countries with the lowest incidence rate of 2.32 per 100,000 (12). Epidemiological studies in Kenya have focused on other types of cancer such as breast cancer, cervical cancer, with minimal mention or identification of EMC (13).

Classification of Endometrial Cancer

EMC is classified based on two aspects, one of which is the appearance of the malignant cells under the microscope (1), which is referred to as the histopathological method (14). In this classification, there is type 1 EMC that represents the less aggressive and rarely spread to non-endometrium tissues (14). There is also type 2 EMC, which has a high chance of spreading outside the uterus (15). Type 1 EMC has cells in glands that appear similar to those of a normal endometrium (16). This type of cancer may have glandular cells and squamous cells, in which case it is referred to as adenocarcinoma. Malignancy in the glandular and squamous cells changes their name to adenosquamous carcinomas(17). Type 2 EMC represents the less common endometrial cancers. Unlike the type 1 EMC, which is majorly caused by excess estrogen, the cause of type 2 cancer is unknown (17). Apart from type 1, other EMC cancers fall under the

type 2 category. The appearance of type 2 EMC does not resemble the normal uterine tissue and has poor differentiation (17).

The second classification is based on endocrine and clinical features (14) into grades 1, 2, and 3 (1). Grade 1 and 2 refer to the lower-grade cancers and are type 1 EMC while grade 3 refers to the high-grade cancers and are type 2 EMC (1). The grading is based on the organization of cancer cells into glands that resemble glands of a normal endometrium (1). In this case, the lower-grade cancers have malignant cells that form glands while the higher-grade cancers have cells that are disorganized and do not form glands. In more specific terms, grade 1 patients contain tumors with 95% of cells forming glands. Grade 2 have between 50% and 94% cells forming glands while grade 3 have less than 50% of cells forming glands.

Importantly, histopathological features provide six major types of EMC, including serous carcinoma, adenocarcinoma, small cell carcinoma, uterine carcinosarcoma, transitional carcinoma, and squamous cell carcinoma (18). There are other less common EMC types such as mucinous adenocarcinoma, clear-cell carcinoma, undifferentiated carcinoma, and serous adenocarcinoma (18). The less-common EMC types normally grow and spread fast and can move outside of the uterus before diagnosis. The American Cancer Society refers to this as type 2 endometrial cancer (1). However, the most common EMC is adenocarcinoma, which has sub-classifications. The most common adenocarcinoma is endometrioid cancer, which begins in the gland cells and resembles normal endometrium (18).

The prognosis of EMC is dependent on histological type. The stage-1 disease carries a 5-year survival rate of 86%(19). Type II, which is characterized by more aggressive tumors, early invading myometrium and vascular spaces, with associated advanced-stage disease and higher

tumor grade non-endometrioid histology carries a high mortality rate compared to type 1(20). The histological grade is strongly associated with prognosis, stage, lymph node metastasis, and myometrial invasion(20). Nonendometrioid carcinomas are considered high-grade tumors and thus need not be graded. Patients with grade 1 tumors have a five-year survival rate of 94%, grade 2 tumors have a five-year survival rate of 84% while grade three has a survival rate of 72% (21). Boronow et al. reported 5-year survival 81% in stage I, grade 1 patients, and 50% in stage I, grade 3 patients(22).

Risk Factors for Endometrial Cancer

Andorieh et al (23) in a case-control study identified the risk factors for EMC as obesity, family history of reproductive cancer, nulligravidity, and nulliparity. Based on these findings, women who have never given birth are at a higher risk of EMC than their parous counterparts as supported by Wu et al (24). The number of pregnancies experienced by a woman is also a risk factor of EMC where women with fewer or no pregnancies being at higher risk (23). Nulliparity and nulligravidity relate to the third risk factor of history of infertility. History of infertility may mean that such women have undergone multiple fertility treatment options using drugs that increase the risk of developing EMC (23).

A family history of reproductive cancer is another significant risk factor. Win et al. connect a family history of cancer and an increased risk of EMC (25). In the case where a woman has a first-degree relative with a diagnosis of EMC under 50 years, there is a high chance of developing EMC (26). The risk increases with an increase in the number of first or second-degree relatives with EMC. Family history points to the presence of inherited gene mutations.

The majority of inherited cases are associated with hereditary nonpolyposis colorectal cancer (HNPCC) also Lynch syndrome (27). Lynch syndrome is an autosomal-dominant inherited cancer susceptibility syndrome that is caused by a germline mutation in one of the DNA mismatch repair genes (28). Women with Lynch syndrome have a 40-60% chance of endometrial cancer as the first clinical manifestation(29).

Obesity is associated with a risk of EMC, where women with a body mass index (BMI) of more than 25 are at higher risk (30). An increase in BMI increases the risk of EMC and according to Crosbie et al (31), a BMI of more than 45 increases the risk of EMC by 9.11 times compared to those with a BMI of 18.5 – 24.9 (31). In support, Bhaskaran et al. linked 41% of EMC cases to being overweight or obese (32). In addition, these authors suggest that of the twenty most common types of cancer, EMC has the highest correlation with excess adiposity (32). Obesity leads to increased risk of EMC because the excess adiposity causes the body to release excess estrogen, resist insulin, and develop inflammations (26).

Age is also a risk factor for EMC. Women who are post-menopausal are more likely to develop EMC (33). More than 85% of cases of EMC occur after 50 years. A low percentage (about 5%) of cases are reported below 40 years and such cases majorly occur in young women with excess adiposity, genetic predisposition, or anovulatory cycles (33). Aging leads to changes in the levels of reproductive hormones, which then redefines the endometrium status. The level of estrogen increases in the perimenopausal period. In addition, with the cessation of ovulation, the production of progesterone drops. Progesterone is protective in reference to endometrial cancer. These lead to unopposed estrogen stimulation of the endometrium, which increases the risk of EMC(34).

Pathophysiology of Endometrial Cancer

The endometrium is a specialized tissue in the uterine cavity which, during the reproductive years, undergoes significant structural changes during each menstrual cycle (35). The endometrium is stimulated by trophic hormones cyclically to undergo normal growth and eventually be transformed into a secretory endometrium with active mucin secretion. The two hormones controlling the endometrial cycle are estrogen and progesterone. Estrogen causes growth (proliferative phase) and progesterone causes luteinization and mucin secretion (secretory phase)(36). It is clearly understood that excessive estrogen production will lead to overstimulation of the endometrial stratum functionalism and if normal secretory phase endometrial changes do not occur under the influence of progesterone regular shedding of the endometrium is absent which may eventually lead to hyperplastic and malignant changes (36).

The pathophysiology of EMC differs according to type. About 80% of EMC cases result from histologic endometrioid morphology (37). Type I EMC have a thickened endometrium because of lesions known as endometrial intraepithelial neoplasia (33). As noted earlier, type I EMC has grade 1 and grade 2 tumors. Grade 1 cancers are found to have less than 5% solid components and are well differentiated. Grade 2 has 5-50% solid matter and grade 3 cancers have over 50% solid components.

Type 1 cancers show microsatellite instability and mutations in *CTNNBI*, *PTEN*, *KRAS*, and *PIK3CA* genes (38). Type 1 cancers are mainly associated with obesity; the excess adiposity leads to the excessive presence of estrogen because of increased peripheral aromatization of androgen (39). Too much estrogen stimulates the proliferation of the endometrium and the excess growth may cause gene mutations. Persistence in mutation as a result of disturbance of

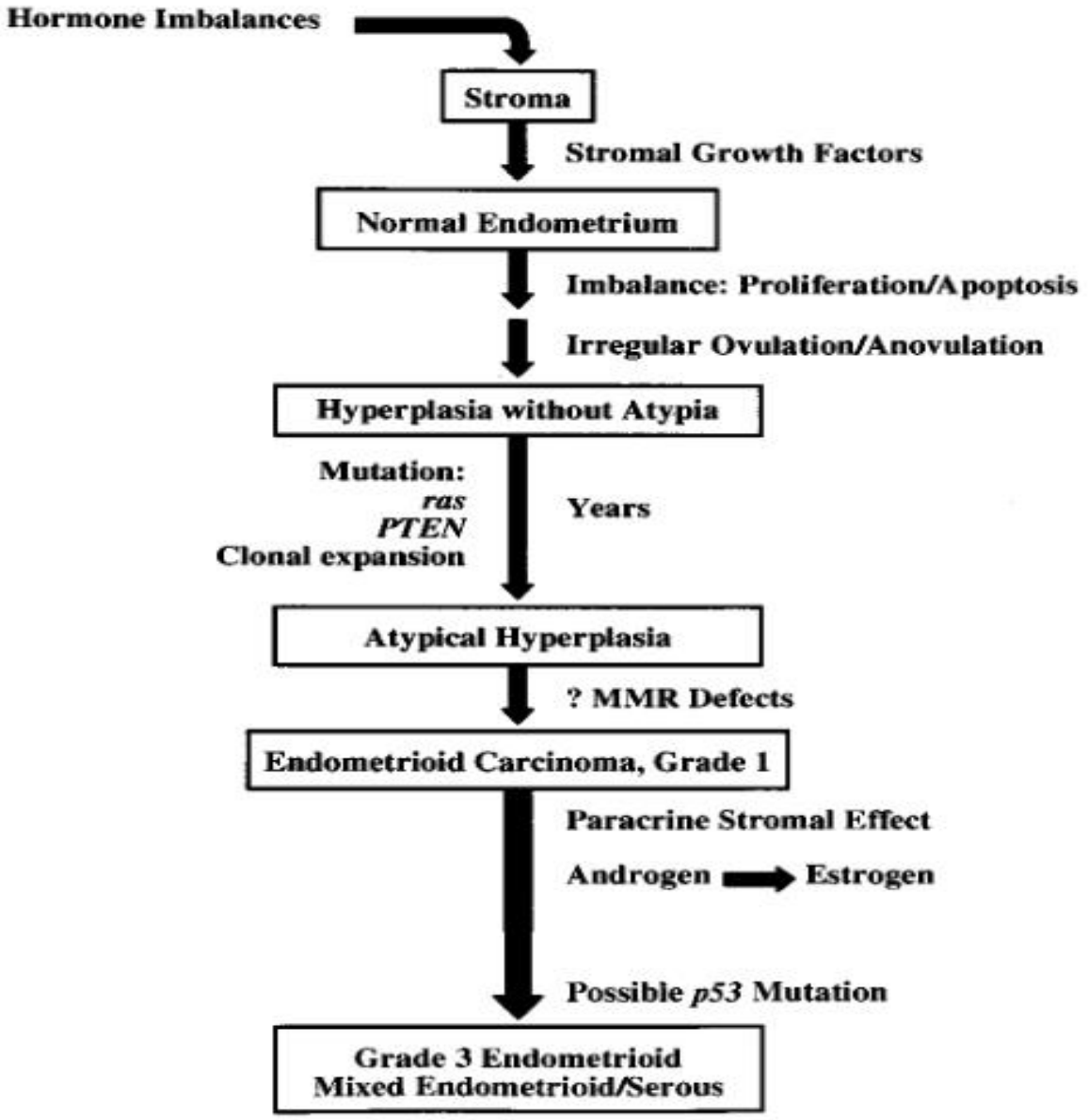
the apoptotic pathway causes the multiplication of these cells forming EMC (40). Type II cancers, on the other hand, tend to have *p53, p16, TP53,* and *ErbB2* mutations and are highly likely to develop deep myometrial invasion and lymph node metastases (38). Unlike the type, I cancer, type II cancer does not depend on estrogen for growth, but rather develop in an atrophic endometrium (41).

Relevant Models on Endometrial Cancer

This study is guided by the dualistic model of endometrial cancer proposed by Sherman (42). This is a model based on the understanding that EMC develops from excess estrogen exposure or atrophic epithelium. Sherman proposed a model that combines an estrogen-based classic pathway (***Figure I***) and an alternative pathway (***Figure II***) that does not relate to hormones.

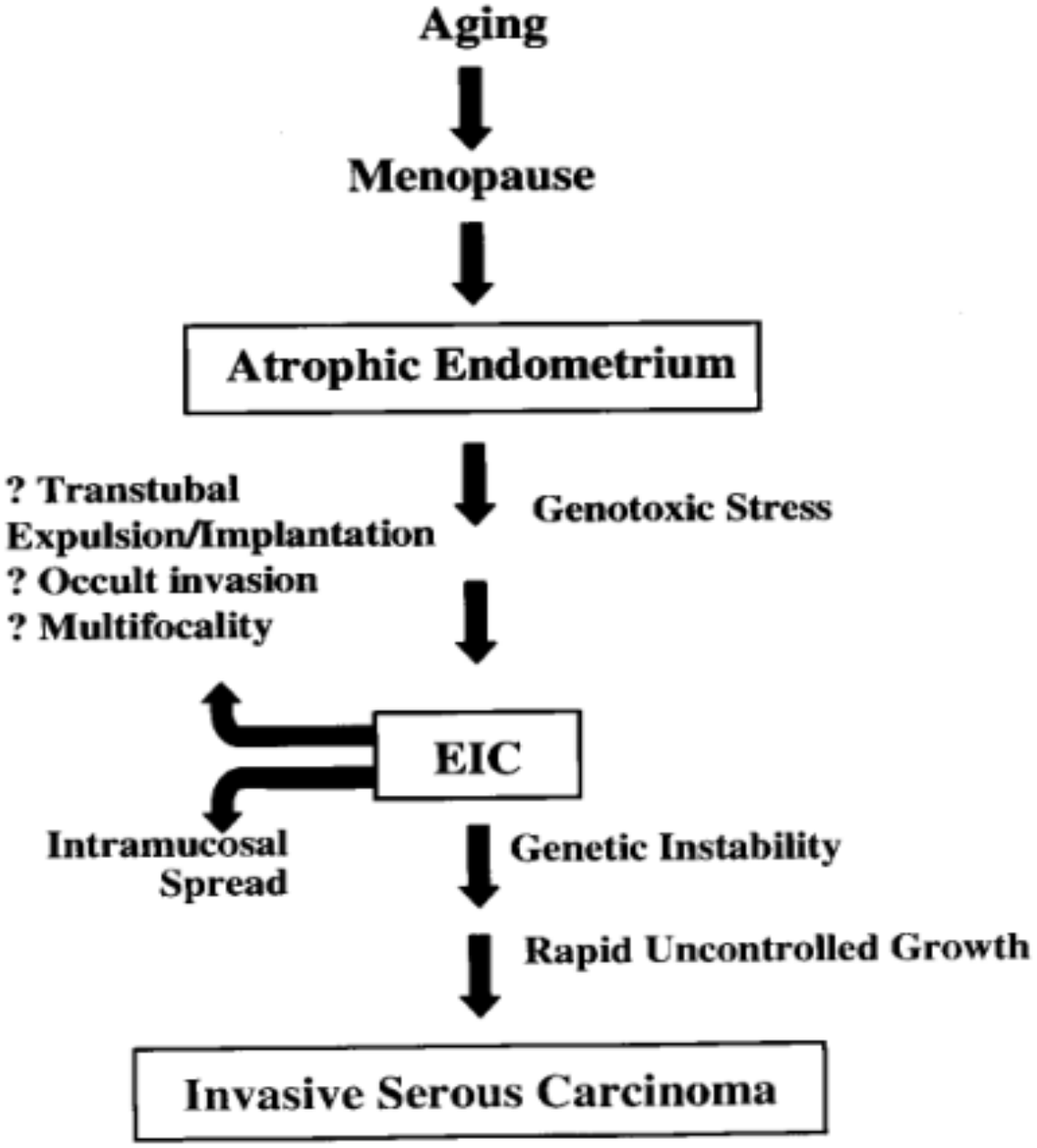
The classic pathway guides the management of type I EMC, whereas the alternative pathway guides management of type II EMC. Type 1 EMC does not depend on patient comorbidities but rather hormonal imbalances while the alternative model shows the importance of patient morbidities (42). Understanding the clinical presentations, best management approaches, and survival rates need to consider the pathway for EMC development and the dualistic model is a good fit.

Figure 1:Type I Pathway



Source: Sherman, 2000; p. 304

Figure 2: Type II Pathway



Source: Sherman, 2000; p. 305.

Assessment and Diagnostic Approaches

The assessment of EMC is somewhat not similar to that of other types of cancers. Routine screening is not recommended (43). Moreover, the reliability of Pap smear in EMC detection is low, unlike in cervical cancer screening (44). In addition, the use of transvaginal ultrasound in women with no clear symptoms is not recommended because of the unnecessary biopsies that result from false-positive results (33). The recommended assessment for EMC is clinical presentation. This starts with examining the history of the patient to identify symptoms and associated risk factors (33). A family history of reproductive cancer helps to identify whether a patient is susceptible based on hereditary reasons (33).

Majority of patients (over 90%) present with uterine bleeding with abnormal discharge (45). Post-menopausal bleeding can be an indication of EMC and thorough evaluation should be done to rule it out. Research has shown that 10% of biopsy tests for vaginal bleeding post menopause reveal EMC (45). Assessment may also involve imaging using transvaginal ultrasound that reveals thick endometrium. This might also give information on the characteristics of the endometrium. There is no need for biopsy in symptomatic patients with a thin endometrium (<5mm). Pyometra, which is an infection in the uterus often due to hormonal changes, is a condition to look for while assessing EMC (33).

Once the clinical history is complete, the physical examination should be done. It is important to note that early disease stages appear normal and the physical exam might appear normal. The examiner can palpate the inguinal or supraclavicular lymph nodes (46). An abdominal examination to check firmness which indicates infiltration of the omental fat by the material of soft tissue density, and the presence of ascites (33). Speculum assessment is done to check how

the vagina and cervix appear in terms of tumor protrusion in the latter and involvement of the former (33). Uterine mobility and size together with enlarged adnexal structures are assessed using bimanual pelvic examinations (33).

Confirmation of EMC is done through a biopsy examination of the endometrial lining. Examiners might perform the biopsy during the pelvic examination. Dilation and curettage are recommended if biopsy findings are negative. Confirmed diagnosis of EMC should be followed by imaging such as computed tomography (CT) scanning or magnetic resonance imaging (MRI) to rule out metastatic diseases and evaluate the extent of EMC. Assessment of an EMC patient preoperatively helps in the determination of the best surgical methods. Evaluation of patient comorbidities is crucial during the assessment process (33).

Management Approaches

There are various approaches recommended for the management of EMC. The most common and frequently used techniques include sentinel lymph node mapping, surgery, risk stratification, adjuvant therapy, chemotherapy, novel therapeutic techniques, and hormonal therapy.

Sentinel Lymph Node Mapping

This approach is appropriate when EMC is confined to the uterus (6). It assesses the pelvic nodal basin through dye injection into the cervix that a surgeon uses to follow the lymphatic pathway and potentially identify metastases (46). Indocyanine green is recommended as the injection dye for its high detection rate(33). The technique works well when there is suspicion of EMC because it is able to easily detect metastases in the lymph nodes. A limitation of this technique, however, lies in its dependence on the accuracy of the dye. In case the dye is inaccurate, then the

detection of metastases will not be successful. Fortunately, the technique is still new and its role needs further evaluation (33).

Surgery

Surgery is the key management approach for EMC. The surgical approach involves TAH and BSO procedures alongside an assessment of the lymph nodes. The extent of surgery for EMC depends on the stage of the disease. The TAH surgical procedures entail removing the cervix and uterus while the BSO involves removing the adnexa (ovaries plus fallopian tubes) (33). Minimally invasive techniques can be used to remove these reproductive organs and thus reducing the length of hospital stay and associated complications (33). During the above surgical procedures, lymph node assessment is done to check for enlarged nodes, especially for patients with high-risk histology such as high-grade endometrioid, serous, and clear cell carcinomas. This assessment helps surgeons to rule out metastatic nodes. It is important to note that the surgical technique of TAH and BSO with lymph node assessment is effective for uterus-confined EMC. Therefore, there is a need to thoroughly examine the abdomen for a chance of EMC having metastasized from the uterus (33).

Adjuvant Therapy

Adjuvant therapy, both chemotherapy, and radiotherapy are complementary to the primary treatment. The management approach aims to reduce EMC recurrence for a new diagnosis. Its use is recommended by surgeons based on disease staging, histology typing, and associated risk factors (6). High-risk histology, the involvement of the cervix, and myometrial invasion increase

the chance of adjuvant therapy recommendation (47). Type II cancers might require adjuvant therapy regardless of staging considering their high-risk nature.

Radiation Therapy (RT) techniques

The RT is the most frequently used adjuvant technique for EMC management (48). It applies in the adjuvant care and to patients in palliative care, those who cannot undergo surgery, and in cases where EMC recurs locally (49). Its delivery method includes vaginal brachytherapy (VBT) or external beam radiotherapy (EBRT), the former of which is a low morbidity treatment option while the latter has acute side effects (50). It is important to note that the use of adjuvant RT is reducing overtime because of advancements in surgical staging (33). In a report of 162 stage II endometrial carcinoma patients, the 5-year disease-free survival was improved (94% versus 76%) in patients who underwent radical hysterectomy(51). Another study by Wright et al. assessing 1577 women with stage II endometrial adenocarcinoma assessing the prognosis for those receiving hysterectomy with or without radiation showed that without radiation, women who underwent hysterectomy were 48% more prone to death (52).

Chemotherapy

Chemotherapy is reported to minimally affect EMC cells compared to RT (33). However, it is an important management approach when EMC is recurrent or in an advanced stage. It's a technique highly recommended for high-risk histology, especially type II cancers. The goal of chemotherapy is to limit the aggressive nature of type II cancers, hence reducing the chances of developing extra-uterine diseases (53). A combination of carboplatin and paclitaxel is often prescribed for advanced EMC primarily due to its manageable toxicity and the fact that the

combination has a high response rate of between 64–78% (51). However, evidence indicates that chemotherapy alone in managing EMC has been linked to pelvic relapse rates of 18% to 47% (51).

Hormonal Therapy

Estrogen enhances epithelial proliferation while progesterone causes epithelial differentiation. In achieving the anti-tumor effect, progestins stimulate differentiation of tumor cells in addition to the activation of apoptotic pathways or block active cell division(54). Often, hormone therapy is used when dealing with type I cancers with well-differentiated tumors. It is recommended for patients with grade I tumors (55). It is a successful technique for patients with low incidences of tumor recurrence. According to Passarello et al (33), clinical trials have yet to establish a superior hormone. However, progestin is the primary and recommended agent for hormonal therapy. Therapy using progestin is given majorly as medroxyprogesterone acetate. Hormonal therapy is not a guarantee for patients' recovery, thus, close monitoring should be done to assess the disease prognosis (56). Hormonal therapy is often preferred for frail patients for the fact that it has minor adverse effects compared to chemotherapy(54). Surgery should be done with staging 12 months after hormonal therapy (33).

Novel Therapeutic Techniques

Novel therapeutic techniques include the use of therapeutic agents that target EMC tumors at the molecular level (57). Many agents have been tested in clinical trials, but their lack of success and contradicting findings limit their recommendations. Bevacizumab has had the most success when used to maintain a disease-free state for EMC survivors. Agents such as metformin show

improvement in the mortality rate for cancer patients. However, novel agents should be explored more in clinical trials to provide insight into their success (58).

Management of EMC at KNH

The Kenya national cancer treatment protocols 2019 outlines the recommended treatment plan to be offered to patients diagnosed with EMC. Different histological types and grades of disease undergo TAH BSO with follow up including radiotherapy with or without additional chemotherapy using Carboplatin/Paclitaxel based regimes.(59)This is the strategy applied to patients managed in KNH with patient-specific characteristics considered in the management of patients. Staging is done during surgery and the uterus is taken for histological grading of disease. Peritoneal washouts are not routinely taken especially in the absence of ascites. Patients are followed up in the clinic monthly for three months then six-monthly for two years and annually over the next three years. During follow up in the clinic, patients are evaluated to rule out recurrence, and if present chemotherapy or hormonal therapy may be administered.

Prognosis and Survival Rates of Endometrial Cancers

Histology and stage of the tumor determine the prognosis of EMC. In addition, lymph node status, cell type, age of the patient, and myometrial penetration are key prognostic factors (60). Improvement of the disease is registered in early staging and survival is higher in early stages compared to advanced stages. Research has shown a higher 5-year relative survival rate for early surgical stages. For example, the American Cancer Society has shown that localized stages have a survival rate of 96% compared to the distant stage with 18% (61). Based on histology, type 1

EMC is likely to improve compared to type II cancers. Type II is in the advanced stages while type I is in the early stages, meaning that the latter has a better prognosis than the former (33).

Complications of Endometrial Cancers

After the treatment of EMC, the patient might develop complications mostly in the urinary and cutaneous systems. Complications may also affect the small bowels, lower extremities, and rectum (62). Piovano et al. reported that 25% of women treated with EMC develop complications (63). The use of lymphadenectomy as a treatment option leads to lymphedema and lymph cysts (54,(65). Postoperative complications of EMC relate to patient comorbidities and patients with conditions such as diabetes and obesity are more vulnerable (66).

CONCEPTUAL FRAMEWORK

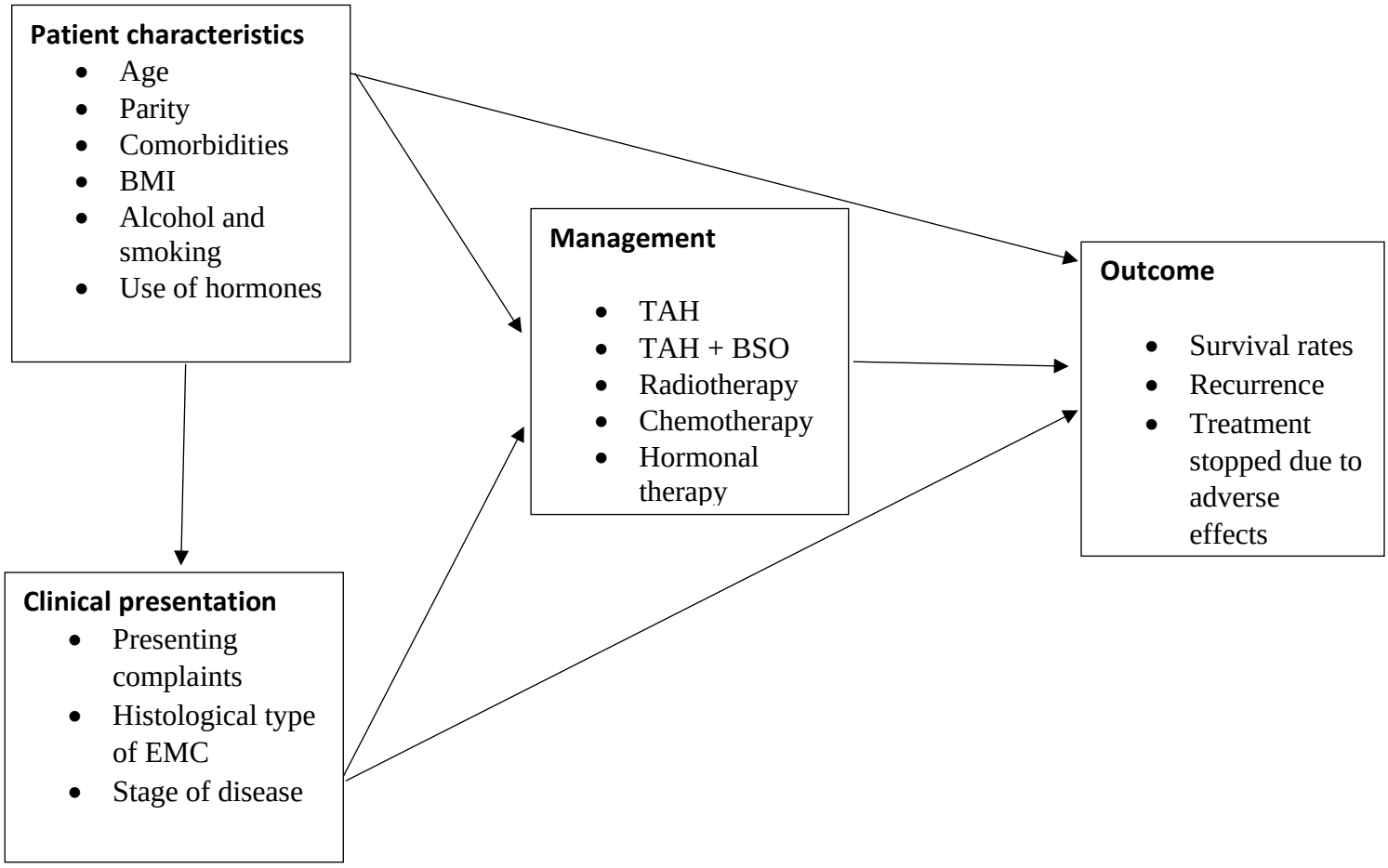
The conceptual framework illustrates the interaction between the major variables involved in this study. There are four broad components highlighted in the framework, which include socio-demographic factors, the clinical presentation of the condition, management of EMC, and the outcomes. Demographic factors such as age, parity, BMI, and menarche have a significant influence on the management regime, the clinical presentation, and the outcome. For instance, the dosage for hormonal therapy, adjuvant therapy, chemotherapy, and radiotherapy used in managing EMC is often calculated based on factors such as patient age, BMI, comorbidity, and inconsideration of patient occupation (especially where sedation is involved). The outcome of the management, which would include factors such as adverse effects experienced is more likely to be pegged on the patient's health (BMI, comorbidity, physical activeness), age (the elderly are more prone to adverse side effects from chemotherapy), and social support such as from family members (gravidity).Age at menarche determines the total time of exposure to reproductive hormones, which can influence the age at which EMC sets in.

Management, which entails the different options available for managing EMC have a profound influence on EMC outcomes, yet the choice of care is dependent on clinical presentation and the demographic factors. For instance, chemotherapy, radiotherapy, hormonal therapy, and surgery may have a different outcome of survival rates and adverse effects across different patients. The decision on which management to adopt is highly influenced by the severity of the condition (clinical presentation).

The outcomes, as has been mentioned earlier include morbidity (complications), adverse effects, and mortality rates. These are influenced by demographic factors, clinical presentations, and

management options. For instance, a clinical presentation that depicts an invasive EMC scenario may have low odds of survival as compared to one in the early stages other factors held constant. Therefore, all the four major categories (demographic factors, management, clinical presentation, and outcomes) are interlinked; thus, the conceptual framework is best suited to create a pictorial illustration of the influence each of the categories has on the others as illustrated in ***Figure III*** below.

Figure 3: Conceptual Framework



JUSTIFICATION OF THE STUDY

Although the prevalence of endometrial cancer is lower in African than in the Western population, the condition accounts for significant mortality and morbidity. Some studies (13,15) have hypothesized that the reported low prevalence of endometrial cancer in Africa is mainly a result of under surveillance of the disease rather than actual numbers. According to the 2019 UN world mortality report, the average life expectancy in developed countries was 80 years compared to 61 years in Africa. This may also be a factor in the lower rates of EMC in the African population.(67) The available data and the management protocol for EMC are based on studies conducted in western countries. These countries are much more developed with state-of-the-art cancer units and advanced technology compared to the situation in Kenyatta National Hospital (KNH), in Kenya. Therefore, continued reliance on such evidence from two distinct settings (culturally, resource-wise, and health literacy level) may not offer a holistically transferable approach. There is insufficient information on EMC in Africa and in Kenya to be precise. There is a paucity of information on socio-demographic characteristics, clinical presentation, and outcomes of EMC patients at KNH. Lack of locally available data may compromise the possibility of establishing an evidence-based practice that is locally engendered.

Despite the lack of precise data on the prevalence of endometrial cancer in Kenya, hospital-based data indicate that for every 30 cases of cervical cancer, there is one case of endometrial cancer. With cervical cancer in Kenya accounting for 8 – 20% of all cancer cases, an incidence rate of 2,454, and death estimates of 1,676 women annually, the burden of EMC cannot be ignored (68). This study focussed on analysing data on EMC at the KNH oncology centre with the purpose of addressing the gaps of locally available data. In this study, the sociodemographic characteristic

of EMC patients, and outcomes (morbidity, mortality, - and survival at two years and five years) was analysed. The study is necessary at this point in time to help in delivering quality care, setting preventive strategies, and understanding the nature of the disease from locally informed data. The data collected will also play a crucial role in defining the condition in the Kenyan context based on the demographic characteristics of patients diagnosed with EMC. By presenting this data, the study aims to raise awareness on EMC for both healthcare providers and the general public. In the end, the study will contribute towards building the body of literature and make it possible to compare disease characteristics and treatments between Kenya and other countries. Ultimately, the findings from this study may come in handy in policy formulation as regards endometrial cancer or eliciting a chain of future studies on the condition that can result in better understanding and improvement of care models

RESEARCH QUESTION

What are the clinical characteristics and treatment outcomes of patients managed for endometrial cancer in KNH, 2012-2018?

RESEARCH OBJECTIVES

Broad Objective

To evaluate the clinical characteristics and treatment outcomes of patients managed for endometrial cancer in KNH, 2012 -2018.

Specific Objective

Among patients managed for endometrial cancer in KNH, 2012-2018 to:

1. Describe the clinical characteristics and the histological types
2. Determine treatment offered
3. Determine the recurrence and remission rates
4. Determine the two- and five-year survival rates

METHODOLOGY

Study Design

This was a descriptive cohort study using routinely collected data. Phone calls were used to obtain missing data. The study population was made up of women diagnosed with EMC. Their disease course over a maximum of five years was evaluated, and outcomes (remission, recurrence, and survival rates) assessed. The study design allowed a description of the clinical characteristics of patients with EMC because a sample representative of patients seen at KNH could be obtained. Furthermore, the use of secondary data is appropriate in this case because of the detailed information required and the fact that EMC is a rare disease.

Study Site and Setting

The study was conducted in the Medical Records Department of KNH. KNH is located in Nairobi City County, the capital city of Kenya. KNH is the biggest referral hospital in Kenya and the East and Central Africa region. The hospital was founded in 1901 and serves as the teaching hospital for the University of Nairobi. The hospital is situated west of Nairobi's central business district and has a bed capacity of about 2000 beds. The hospital serves close to 70,000 inpatients and 500,000 outpatient clients in all departments annually(69).

KNH has several specialty departments, among them the obstetrics and gynecology department, under which the gynecological unit (the gynae-oncology ward and the outpatient gynecology clinic) operates. Gynecology oncology departments serve about 1,100 cases annually. There are two theatres dedicated to the gynecology department with two days set aside for gynae-oncology patients. The hospital has laboratory technology to undertake histologic diagnosis and has gynae-

oncologists who manage cases of EMC. KNH handles cases referred from different parts of the country, and it is the gynae-oncology center of choice for those seeking health care services in public hospitals in Kenya. It would thus provide a suitable representation of the demographic characteristics of EMC patients in Kenya. Furthermore, the hospital has a well-organized and managed record registry, which makes it easy to retrieve patients' files, thus, facilitating a smooth data collection process.

Patients diagnosed with EMC in KNH are managed based on patient-specific characteristics. However, the commonest management offered is TAH and BSO often without the need for further therapy. Patients are then followed up in the clinic monthly for three months then six-monthly for two years and annually over the next three years after which they are discharged from the clinic after five years if they are considered to have had complete remission.

Study Population

The study population was women, aged 18 years and above, with histologically confirmed EMC, managed at KNH between the years 2012 and 2018. Histological diagnosis was essential in this case to ascertain the cancer diagnosis and, therefore, avoid the inclusion of misdiagnosed cases. The cut-off age of 18 years was so as to include only participants who are old enough to give consent. Only women whose condition was managed at KNH were included because the study relied on patient records. Patients managed primarily in other facilities who presented to KNH for specific follow up services were excluded. Those with other cancers were also excluded because it would have been difficult to disaggregate the effect of EMC on the outcome, especially survival, from that of other cancers.

The inclusion criteria included;

a. Patients aged 18 years and above
b. Patients with a histologically confirmed diagnosis of EMC
c. Those whose condition was managed at KNH

The exclusion criteria included;

a. Those with other cancers
b. Those who, when contacted by phone, declined to take part in the study were excluded secondarily.

Sample Size Calculation

Data obtained from the oncology department (see ***Box I***) indicates that for the years 2012 through 2018, the total number of endometrial cancer was 327 in 4283gynaecological cancer cases. The sample size was calculated using the formula; $N = \frac{P}{1+Pe2}$ that was developed by Yamane Taro in 1967. (59, p33) where;

N = sample size, **P** = population of the total number of cases during the targeted period, which is **327**, and **e** = significance level, which is **0.05.** A 10% of the sample to be added as cushion for files likely to be eliminated on technicalities such as missing or inadequate data.

$$n = \frac{327}{1+327(0.05*0.05)} = \mathbf{180}$$

Adding 10% (n = 18), the resulting sample size will be **N =198 participants**

Box 1: Data from the Records Department

Year	Reproductive Tract Cancer	Endometrial Cancer Cases	Sample **(p/P)N**	**n =**
2012	694	44	27	
2013	258	14	8	
2014	711	56	34	
2015	638	21	13	
2016	661	42	25	
2017	552	55	34	
2018	769	95	57	
Total	**4283**	**327**	**198**	

During data collection, only 68 cases met the criteria for the study. Given the low number, all eligible cases were recruited. A detailed description of the selection process is described in the results section.

Sampling Technique

Participants were recruited sequentially from the available cases, starting from the year 2012. All cases meeting the criteria were used. The sequential sampling technique was considered appropriate because of the low number of available cases.

Study Variables

Box 2: Variables per objective

#	Objective	Variables	Source of Data
1.	Describe the clinical characteristics and histological types	• Age • BMI • Parity • Years since menopause • Menstrual history (regular or irregular) • Family planning methods used • Histological type • Disease stage • Comorbidities	
2.	To identify management approaches offered	• TAH, • TAH/BSO, • TVH, • Vault radiation, • EBRT, • Chemotherapy, • Hormonal therapy combination	Medical records review and phone calls
3.	Evaluate treatment outcomes	• Complete remission, • Recurrence, • Stopped for adverse effects	
4.	Determine the two- and five-year survival	• Years lived since diagnosis of EMC	

Data Collection and Management

Data Collection Tool

Data were collected using a pre-developed and appraised data abstraction form ***(See Appendix B)***. The researcher pre-tested the tool before commencing the actual data collection to ensure that

the tool is valid and reliable. The study tool contained sections for demographic data, characteristics of disease at diagnosis, risk factors, management, and outcomes.

Data Collection Procedure

The researcher, working with two trained research assistants, identified the appropriate patients' files from the oncology department registry. The research assistants were holders of a diploma in Clinical Medicine. Using the file particulars, the files were retrieved from the KNH records and information center. Using the data abstraction form data were abstracted. were abstracted from all available medical records including doctors' notes, nursing cardex, treatment sheets, laboratory and diagnostic reports, referral letters, and any other relevant reports in the files. Each patient data was entered into a respective copy of the study tool with a unique study number. The forms were checked for completeness. Telephone numbers of participants or their next of kin was obtained from the files. Written consent allowing the use of patients' contacts was obtained from the KNH records department (***See Appendix D)***.Those with missing data were contacted by phone. The purpose and process of the study was explained to those contacted and consent sought. If they were willing to participate, a telephone interview was done.

Data Management and Analysis

The data collected was stored and safeguarded under the care of the principal investigator. The data abstraction forms were stored in a lockable locker. The computer where the data was stored in an excel sheet once transferred from the paper form was password protected. Access to both the physical and the softcopies of the data was highly regulated and limited to the researchers, data analysts, and research assistants.

The analysis was done using the Statistical Package for Social Sciences (SPSS) version 24 software. The analysis entailed running both descriptive and inferential analysis to fully respond to the study objectives. The descriptive analysis included means, standard deviation, and percentages. This was presented in the form of a table for comprehensive interpretation. The Kaplan Meier product-limit method was used to estimate survival rates.

Quality Assurance Protocol

Research assistants had to meet the baseline qualification of being holders of diploma or degree in health-related courses and having worked in the hospital setting for at least two years. This ensured familiarity with medical terms and the health system. Also, they underwent adequate training aimed at understanding the research protocol and carrying out the data collection process in a standard way. The data collection tool was pretested with 10% of the targeted samples for authenticating the study tool's completeness, feasibility, validity and reliability. The data was checked daily for completeness and accuracy and corrected accordingly.

Ethical Considerations

Approval to carry out the study was sought from Kenyatta National Hospital/University of Nairobi Ethics and Research Committee (KNH/UoN ERC). The researcher sought permission from the KNH administration to access patients' files and extract relevant data. Approval to use participants' contacts were obtained from the KNH records department. The purpose of the study was explained to participants contacted by phone and consent sought (*See Appendix A*). Patients' privacy and confidentiality was upheld by ensuring the data collection tool contained no identifying information. Study numbers were used in entering data. In addition, the data was

stored in lockable lockers or password-protected computers accessible to only the researchers and research assistants. No patient identification details were used during data analysis and dissemination. The study did not pose any risk to the participants given that it evaluated already documented care as opposed to introducing or evaluating care prospectively.

Study Assumptions and Limitations

The researcher assumed that the available data at KNH was adequate to draw concrete and reliable deductions. A major limitation was the extremely low number of participants in the study. This spoke to the rarity of EMC IN Kenya. Another limitation was mainly on the study design, given that the researcher relied mainly on secondary data, which was not in the exact format required. This was mitigated by comparing data across different reports (medical notes, nurses' notes, laboratory findings, and referral letters) to ensure that the most appropriate inference was made. Also, the researcher made use of the patient contacts provided in the file in cases where there wasa need to make further clarification from the patient regarding inconsistency in data or missing data.

Another possible limitation was selection bias given that KNH is a referral hospital; thus, may not be representative of the general population. However, it is expected that the majority of patients with cancer in Kenya who seek healthcare services from public health facilities would be managed in KNH. This being a retrospective study (where exposure and outcome have already occurred), a third possible limitation was that it may have been difficult to infer the temporal relationship between cause and effect. This was not expected to be a major limitation in this study, because socio-demographic characteristics were assessed on the date the patient was first attended to, at a time when the condition may not have had a major impact on their socio-

economic status. In addition, clinical presentation always precedes outcomes. This study relied on patients' medical records which may be incomplete. To mitigate this, participants whose phone numbers are available were contacted in an attempt to obtain the missing information.

The foreseeable limitations to phone calls as a complementary data collection approach included inaccurate data as it depends on patient recall of specific information from up to eight years in the past. Patients were also be unable to discern specific outcomes especially regarding remission and recurrence. A different disease process may be interpreted as related to initial EMC by the respondent and reported as such. Missing data was a major challenge as some patient's phone numbers were no longer be in use. This was however mitigated by contacting their next of kin.

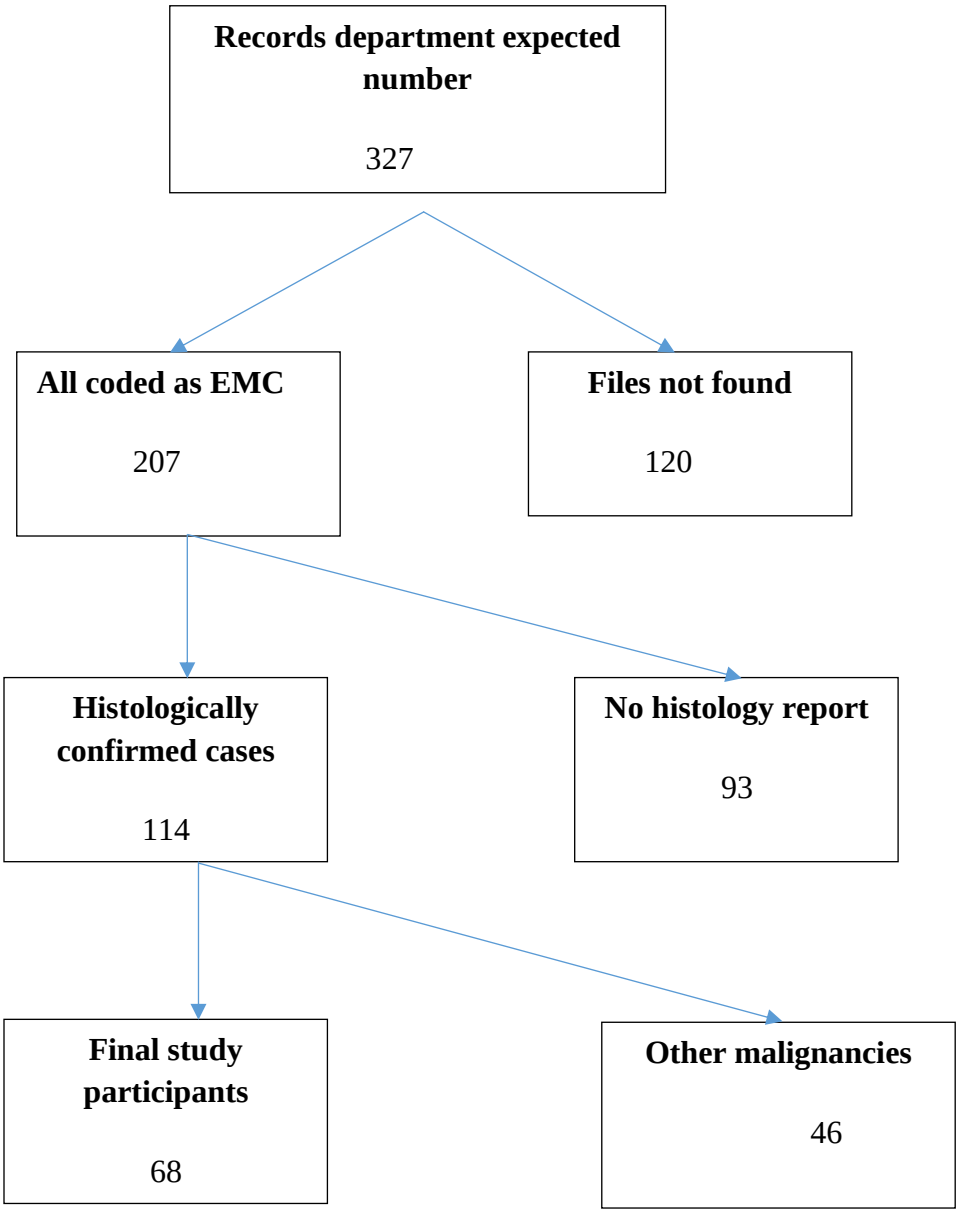
Dissemination of Results

Once the research is completed and the results are established, the researcher will disseminate the findings through publishing hardcopies of the research, having a soft copy of the research in the university repository, and ultimately publishing the findings in an internationally reputable health-related journal. A summary of the findings will be given to KNH with the intention of contributing to current and future policies and guidelines in the identification and management of patients with EMC.

RESULTS

A total of 68 participants were included in this study. Out of the anticipated 327 files, only 207 files were available, 120 files could not be traced. Out of those available, 93 were excluded since no histological report was available to confirm diagnosis. From the remaining 114 cases, 46 cases were excluded because they had other malignancies alongside EMC (Figure 4).

Figure 4: Flow diagram of endometrial cancer patients eligible for analysis, KNH 2012-2018



Demographic and Reproductive Characteristics

A total of 68 women managed for EMC at KNH were included. The mean age of participants was 63.2 (SD = 9.8) years, with a range of 37-87 years. As shown in Table 1, most participants were of married (61.5%), of Kikuyu ethnicity (57.4%), unemployed (56.9%),with a primary education (54.5%),and residents of Nairobi County (38.2%). Most had never smoked (94.4%) nor taken alcohol (94.1%). The average parity and age at last delivery were 5.26 (SD = 2.97) and 33.65 (6.45) years, respectively.

Table 1: Sociodemographic Characteristics of endometrial cancer patients in KNH, 2012 - 2018

		Number (n = 68)	Percentage
Ethnicity	Kikuyu	39	57.4
	Kamba	8	11.8
	Luo	6	8.8
	Luhya	6	8.8
	Others[1]	9	13.3
Occupation	Unemployed	37	56.9
	Self employed	18	27.7
	Formal employment	9	13.8
	Casual laborer	1	1.5
	Missing	3	
Marital status	Married	40	61.5
	Never married	7	10.8
	Widowed	8	12.3
	Single	5	7.7
	Separated	4	6.2
	Divorced	1	1.5
	Missing	3	
County of residence	Nairobi	26	38.2
	Muranga	8	11.8
	Kiambu	6	8.8
	Nyeri	5	7.4
	Others[2]	23	33.9

Others[1] – Kisii, Meru, Giriama, and Embu
Others[2] – Machakos, Nakuru, Kirinyaga, Kakamega, Embu, Kitui, Kilifi, Busia, Mombasa, Kajiado, Kisii, Kisumu, and Trans Nzoia

Obstetric and gynecologic history of patients managed for endometrial cancer in KNH between 2012 and 2018 is presented in Table 2. The average parity was 5 (SD =3). The average age at last delivery was 34 (SD = 6) years, while 27.9% had a history of family planning. The most used family planning method was copper T intrauterine contraceptive device (52.7%), while the most

common comorbidity was chronic hypertension (57.4%). Of the 24 participants with data on weight and height taken for initiation of chemotherapy, most (45.8%) had obesity class I.

Table 2:Clinical characteristics of patients managed for endometrial cancer in KNH, 2012 - 2018

	Mean	SD
Average parity [Mean (SD)]	5.3	2.97
Abortions [Mean (SD)]	0.2	0.57
Age at last delivery[Mean (SD)]	33.7	6.45
	Count (N)	**Percentage (%)**
History of family planning	19	27.9
Copper T coil	10	52.6
Combined oral	9	47.4
Depo-Provera	3	15.8
Tubal ligation	3	15.8
Condoms	1	5.3
Comorbidities		
Chronic Hypertension	39	57.4
Diabetes	17	25.0
Others	9	13.2
BMI		
Normal weight	3	12.5
Pre obesity	8	33.3
Obesity class I	11	45.8
Obesity class II	2	8.3

Others – Asthma, Hypothyroidism, HIV, CCF

Vaginal bleeding (80.9%) was the most common clinical presentation, followed by abdominal pain (38.2%), vaginal discharge (26.5%), and pelvic pain (16.2%), as shown in Table 3.Endometrial adenocarcinoma was the most common histology type (68.2%). Of the 34 who had EMC grading results, a majority (55.9%) had EMC grade 2. Of the 45 who had EMC staging results, a majority were stage I (26.7%) and III (26.7%)

Table 3. Clinical and pathological characteristics of patients managed for endometrial cancer in KNH, 2012 – 2018

		N (68)	%
Clinical characteristics	Vaginal bleeding after menopause	55	80.9
	Abdominal pain	26	38.2
	Vaginal discharge	18	26.5
	Pelvic pain	11	16.2
	Others[1]	35	51.8
Histology	Endometrial adenocarcinoma	45	68.2
	Papillary adenocarcinoma	7	10.6
	Endometrial serous carcinoma	4	6.1
	Squamous cell carcinoma	4	6.1
	Others[2]	6	9.0
EMC grading	Done	34	50.0
	Not done	34	50.0
EMC grade	1	10	29.4
	2	19	55.9
	3	5	14.7
EMC staging	Done	45	66.2
	Not done	23	33.8
EMC stage	I	12	26.7
	II	11	24.4
	III	12	26.7
	IV	10	22.2

Others[1] - Bleeding between periods, Lower Back Pain, Abdominal distension, Irregular menstrual bleeding, Abdominal mass, Persistent bloating, Weakness, DIB, Confusion, Diarrhea, Dehydration, Inability to walk, General body swelling, Dyschezia, Haematochezia, Vaginal mass, Weight loss, and Anorexia

Others[2] - Clear cell carcinoma, Endometrial sarcoma, Endometrial stromal sarcoma, Giant cell adenocarcinoma, Malignant mullerian mixed tumor, Papillary squamous carcinoma

Surgery was the most common treatment modality (96.7%) as shown in Table 4. Of the 59 who underwent surgery, a majority underwent TAH-BSO (83.1%). Chemotherapy, adjuvant therapy, and radiotherapy were required in 54.1%, 13.1%, and 19.7% of cases. Seven participants (10% of the participants) did not receive any therapy after diagnosis. This was because they were not clinically stable enough to withstand any of the treatment modalities available to them. Of these, five had died by the time of data collection.

Table 4: Management of patients with endometrial cancer in KNH, 2012 - 2018

	N (61)	**%**
Surgery	59	96.7
TAH-BSO	49	83.1
Pelvic lymphadectomy	8	13.6
Hysterectomy	3	5.1
Total Abdominal Hysterectomy (TAH)	7	3.4
Bilateral Salpingo-Oophorectomy (BSO)	2	3.4
Omentectimy?	1	1.7
Radical gysterectomy?	1	1.7
Radical mastectomy	1	1.7
Marsupialization	1	1.7
Peritoneal wash	1	1.7
ALND	1	1.7
Chemotherapy	33	54.1
Adjuvant	8	13.1
Radiotherapy	12	19.7

A majority (66.7%) of the participants recovered after treatment as shown in Table 5. The average duration to recovery was 1.8 (SD=1) years, range 1-7 years, while the recurrence rate was 30.6%. For all the participants, the mortality rate at the time of data collection was 28.4%.

Table 5: Treatment outcomes of patients managed for endometrial cancer in KNH, 2012 – 2018

		N (68)	**%**
Recovery from EMC	Yes	44	64.7
	No	21	30.9
	Unknown	3	4.4
Recurrence	Yes	11	25.0
	No	25	56.8
	Unknown	8	18.2
Outcome	Dead	19	27.9
	Alive	48	70.6
	Unknown	1	1.4

Two-thirds (73.3%) of those with endometrioid adenocarcinoma were alive at two years after diagnosis as shown in Table 6. Survival rates were better for those with endometrial serous carcinoma (100%), papillary adenocarcinoma (85.7%), and squamous cell carcinoma (100%). Two-thirds (66.7) of those with endometroid adenocarcinoma were alive at five years after diagnosis.

Table 6: Two- and five-year survival by histological subtypes

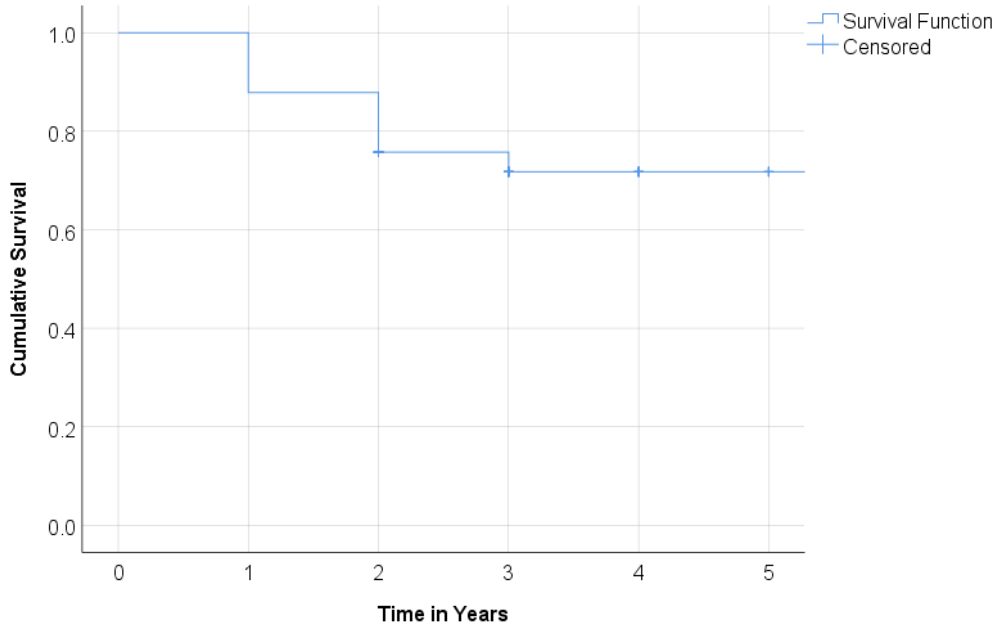
Histology	Alive at Two Years		Alive at Five Years	
	Count (N)	Percentage[1] (%)	Count (N)	Percentage[1] (%)
Endometroid adenocarcinoma (n = 45)	33	73.3	30	66.7
Endometrial serous carcinoma (n = 3)	3	100	3	100
Papillary adenocarcinoma (n = 7)	6	85.7	6	85.7
Squamous cell carcinoma (n = 4)	4	100	4	100
Others2 (n = 6)	4	66.7	4	66.7
All histological types (n = 65)	50	76.9	47	72.3

[1]Percentages were based on the totals of the histological subtype

[2]Others: endometrial sarcoma, clear cell carcinoma, giant cell adenocarcinoma, Müllerian mixed tumor, papillary squamous carcinoma and endometrial stromal sarcoma

Figure 5: Five Year Survival Rates for EMC Patients at KNH from 2012 - 2018

Cumulative survival rate was 75.8% at two years and 71.8% at five years. This is graphically in the Kaplan Meier curve below. (Figure 5)



DISCUSSION

The main findings for this study were that women managed for endometrial cancer at KNH between 2012 and 2018 were generally of an older age group (mean age=63 years), of high parity, unemployed, married and resided in Nairobi. Majority of them (97%) had comorbidities with hypertension being the commonest followed by diabetes mellitus. Slightly above half of them presented with stage I and II disease with the commonest presenting symptom being per vaginal bleeding. The commonest histological type was endometrial adenocarcinoma (68%). Almost all the patients underwent a TAH BSO (83%) and pelvic lymphadenectomy(96%), in addition slightly more than half the patients received chemotherapy (54%) and less than a quarter(20%) received radiotherapy. Overall survival at 2 and 5 years was 76% and 72%, respectively.

From the data, patients were diagnosed with EMC between the 5^{th} and 7^{th} decades of life. The mean age of women with EMC at diagnosis was 63years (SD=9.8). This is comparable with global statistics that indicate more than 85% of cases occur after the age of 50 years as reported by Passarello et al. This is expected as EMC is primarily a disease of post-menopausal women.

The main comorbidities reported were chronic hypertension and diabetes. These patients have frequent contact with healthcare providers which may lead to early discovery of EMC. Metabolic syndrome, a clustering of three or more of five medical conditions; hypertension, diabetes, obesity, high triglycerides and low high-density lipoproteins, is associated with EMC(71). Although this was not specifically assessed, it is likely to have been present in the study participants thus the large number of patients with diabetes and hypertension. Hormonal contraception was not widely used. Vaginal discharge after menopause was reported commonly

in addition to post-menopausal bleeding. Majority of patients had endometroid adenocarcinoma subtype of EMC, found at histological grade 2 in stage 1 of disease. Treatment was provided in most of the cases, primarily TAH-BSO with more than 50% of patients receiving chemotherapy as part of treatment. Sixty seven percent of patients recovered after approximately 2 years of treatment without recurrence. Survival rate was above 70% at both 2 and 5 years. Obesity is a known risk factor for EMC (72). In this study, majority of participants had obesity class 1. However, information on weight was available for only a few participants who underwent chemotherapy. This information on weight and height was taken for initiation of chemotherapy. It was, therefore, difficult to make any inference as to the association between weight and EMC in this study due to the risk of reverse causality.

Vaginal bleeding after menopause and vaginal discharge were the commonest presenting symptoms for endometrial cancer. Even though patients presented with a wide range of symptoms, constitutional symptoms such as malaise, weight loss, and general body weakness were reported but to a less degree. In a systematic review by Hernandez et al. (2015) (73), endometrial cancer commonly presented with abnormal uterine bleeding, especially in women of postmenopausal age. In a comparative cross-sectional study in the USA, Pakish et al. reported a 33-fold and 8.8-fold higher odds of women with endometrial cancer compared to non-cancer patients presenting with vaginal bleeding and a vaginal discharge after menopause. These findings show that women who develop vaginal bleeding or discharge of an unknown origin should consider screening for endometrial cancer, especially if they are post-menopausal. Moreover, screening for endometrial cancer in those with abnormal vaginal bleeding and discharge should be adopted as part of primary assessment of these symptoms. Diagnostic algorithms such as the Norwich DEFAB have been shown to have a high predictive capacity for

endometrial cancer with vaginal bleeding while controlling for diabetes, BMI, age, bleeding frequency, and endometrial thickness (74).

Histology data showed that endometroid adenocarcinoma was the commonest subtype. Aggressive and rare subtypes such as papillary adenocarcinomas and serous carcinomas were less common, with a majority of patients presenting with grade two and stage I endometrial carcinomas. The data is consistent with the findings of Buhtoiarova et al (2015) (75) where a majority of endometrial cancers (85%) were endometroid adenocarcinoma subtype. In a retrospective analysis of 81 Chinese patients (41), endometroid adenocarcinoma was also the commonest subtype. Endometroid adenocarcinoma is a biologically indolent form of cancer with good prognosis in the absence of risk factors such as lymphovascular invasion and lower uterine segment involvement. However, routine monitoring and aggressive treatment, guided by the grade and stage of tumors, is recommended to improve health outcomes.

Treatment was given in 61 out of the 68 cases. Out of the seven women who did not receive treatment, some died before treatment was commenced while others were not fit for intervention due to their clinical status: uncontrolled diabetes and hypertension being the major impediment to surgical intervention. Because a majority of patients had grade 1 and II tumors, in stage I, early surgical intervention proved curative. TAH-BSO was the primary surgical intervention. No minimally invasive surgery was provided for any of the patients. This is in contrast to a study done by Lee et al where it was reported that minimally invasive surgery was gaining popularity in North America. This is due to the fact that during the study period, it was a relatively new management approach and to date is still in its early stages. Pelvic lymphadectomy was required in one out of 10 patients. There is however no consensus on the use of lymph node staging.

Chemotherapy was administered to more than half of the participants, whereas adjuvant therapy and radiotherapy were used in a few participants.

Within two years of treatment after diagnosis, 67.7% of patients recovered from disease. 30.6% of women had recurrence of EMC after initial treatment. This low recurrence rate is due to the higher incidence of type 1 EMC which is comparatively less aggressive. Type 1 EMC often presents as Grade 1 and 2 tumors which have good treatment outcomes.

The cumulative survival rate of EMC was 75.8% at two years and 71.8% at 5 years. This high survival rate is comparable to global statistics. The American Cancer Society reports survival rated of up to 96% for localized disease. According to Frederic et al, high survival rates are due to early presentation and thus early intervention. Vaginal bleeding as a symptom is an early complaint and often alarming in menopause. This leads patients to seek treatment early in the disease and subsequent early intervention. Given that 97% of our study population had comorbidities, there is generally more exposure to healthcare providers in this group than the general population. This is a likely contributor to the good outcomes observed.

The strengths of this study are that it was done in KNH, a hospital that caters for the whole country and the East African region which improves the generalizability of the findings. The long duration of the study (2012-2018) allowed accumulation of cases to evaluate outcomes including survival. In addition, data was obtained from medical record which ensured accuracy. However, the small number of participants limits conclusions regarding outcomes. However, because all eligible cases available were included, the findings are a reflection of the clinical characteristics of histologically confirmed EMC patients managed in KNH between 2012-2018.

CONCLUSION

Characteristics of EMC in Kenya were found to be similar to that seen globally. Vaginal discharge was a common presentation in our population although it is not routinely reported as a major presenting complaint for endometrial cancer in literature. Chronic hypertension and diabetes were the commonest comorbidities reported. TAH-BSO was the primary surgery offered and patients had good overall survival rates, 75.8% at two years and 71.8% at five years.

RECOMMENDATIONS

- Early intervention should be encouraged upon diagnosis as the prognosis is greatly improved by this.
- High index of suspicion should be exercised when faced with post-menopausal discharge even in the absence of bleeding.
- Coding of diagnoses in KNH records department should be done only after confirmation of diagnosis and not on suspicion.
- A study to associate specific risk factors such as metabolic syndrome to EMC should be done.

REFERENCES

1. American Cancer Society. Endometrial Cancer - What is Endometrial Cancer. American Cancer Society. 2019;

2. Hernandez E, Stuart Ferriss J. Endometrial carcinoma. In: Clinical Gynecology. 2nd Ed. Cambridge: Cambridge University Press; 2015. p. 755–68.

3. Center for Disease Control and Prevention. Gynecologic Cancer Incidence, United States—2012–2016. US Cancer Stat Data Br [Internet]. 2019;1(11). Available from: https://www.cdc.gov/cancer/uscs/about/data-briefs/no11-gynecologic-cancer-incidence-UnitedStates-2012-2016.htm

4. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin. 2011;61(2):69–90.

5. Weiderpass E, Antoine J, Bray FI, Oh J-K, Arbyn M. Trends in corpus uteri cancer mortality in member states of the European Union. Eur J Cancer. 2014 Jun;50(9):1675–84.

6. Brooks RA, Fleming GF, Lastra RR, Lee NK, Moroney JW, Son CH, et al. Current recommendations and recent progress in endometrial cancer. CA Cancer J Clin. 2019 May;69(4):258–79.

7. Jane Henley S, Miller JW, Dowling NF, Benard VB, Richardson LC. Uterine cancer incidence and mortality — United States, 1999–2016. Morb Mortal Wkly Rep. 2018 Dec;67(48):1333–8.

8. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA Cancer J Clin. 2018;68(1):7–30.

9. Alshahrani S, Soliman AS, Hablas A, Ramadan M, Meza JL, Remmenga S, et al. Changes in Uterine Cancer Incidence Rates in Egypt. Obstet Gynecol Int. 2018;2018.

10. Joseph A, Olisaemeka EP, Chukwudi OR, Igwe NM, Rose AM. Frequency and Pattern of Gynecological Cancers in Federal Teaching. 2015;4(2):4–7.

11. Macharia LW, Mureithi MW, Anzala O. Cancer in Kenya: types and infection-attributable. Data from the adult population of two National referral hospitals (2008-2012). AAS Open Res. 2019 Oct;1:25.

12. Bohîlțea RE, Furtunescu F, Dosius M, Cîrstoiu M, Radoi V, Baroș A, et al. Evaluation of endometrial cancer epidemiology in Romania. J Med Life. 8(2):218–25.

13. Korir A, Okerosi N, Ronoh V, Mutuma G, Parkin M. Incidence of cancer in Nairobi, Kenya (2004-2008). Int J Cancer. 2015;137(9):2053–9.

14. Murali R, Soslow RA, Weigelt B. Classification of endometrial carcinoma: More than two types. Lancet Oncol. 2014;15(7):e268–78.

15. Talhouk A, McAlpine JN. New classification of endometrial cancers: the development and potential applications of genomic-based classification in research and clinical care. Gynecol Oncol Res Pract. 2016 Dec;3(14):20–30.

16. Setiawan VW, Yang HP, Pike MC, McCann SE, Yu H, Xiang YB, et al. Type i and II

endometrial cancers: Have they different risk factors? J Clin Oncol. 2013 Jul;31(20):2607–18.

17. Abd, Abdou AG, Al-Sharaky DR, Kasem HA. Clinicopathological differences between type I and type II endometrial carcinoma. Menoufia Med J. 2017;30(3):946.

18. Buhtoiarova TN, Brenner CA, Singh M. Endometrial Carcinoma: Role of current and emerging biomarkers in resolving persistent clinical dilemmas. Vol. 145, American Journal of Clinical Pathology. American Society of Clinical Pathologists; 2016. p. 8–21.

19. Gates EJ, Hirschfield L, Matthews RP, Yap OWS. Body mass index as a prognostic factor in endometrioid adenocarcinoma of the endometrium. J Natl Med Assoc. 2006;98(11):1814–22.

20. Uharček P. Prognostic factors in endometrial carcinoma. J Obstet Gynaecol Res. 2008;34(5):776–83.

21. Zaino RJ, Kurman R, Herbold D, Gliedman J, Bundy BN, Voet R, et al. The significance of squamous differentiation in endometrial carcinoma. Data from a gynecologic oncology group study. Cancer. 1991;68(10):2293–302.

22. Boronow RC, Morrow CP, Creasman WT, Disaia PJ, Silverberg SG, Miller A, et al. Surgical staging in endometrial cancer: Clinical-Pathologic findings of a prospective study. Obstet Gynecol. 1984;63(6):825–32.

23. Andarieh MG, Delavar MA, Moslemi D. Risk Factors for Endometrial Cancer. Results from a Hospital-Based Case-Control Study. Asian Pacific J Cancer Prev.

2016;17(10):4791–6.

24. Wu QJ, Li YY, Tu C, Zhu J, Qian KQ, Feng TB, et al. Parity and endometrial cancer risk: A meta-analysis of epidemiological studies. Sci Rep. 2015 Sep;5(14243):01–14.

25. Win AK, Reece JC, Ryan S. Family history and risk of endometrial cancer: a systematic review and meta-analysis. Obstet Gynecol. 2015 Jan;125(1):89–98.

26. Kitson SJ, Gareth Evans D, Crosbie EJ. Identifying high-risk women for endometrial cancer prevention strategies: Proposal of an endometrial cancer risk prediction model. Cancer Prev Res. 2017 Jan;10(1):1–13.

27. Wang Y, Wang Y, Li J, Cragun J, Hatch K, Chambers SK, et al. Lynch syndrome related endometrial cancer: Clinical significance beyond the endometrium. J Hematol Oncol. 2013;6(22):1–6.

28. Meyer LA, Broaddus RR, Lu KH. Endometrial cancer and lynch syndrome: Clinical and pathologic considerations. Cancer Control. 2009;16(1):14–22.

29. Obermair A, Youlden DR, Young JP, Lindor NM, Baron JA, Newcomb P, et al. Risk of endometrial cancer for women diagnosed with HNPCC-related colorectal carcinoma. Int J Cancer. 2010;127(11):2678–84.

30. Onstad MA, Schmandt RE, Lu KH. Addressing the role of obesity in endometrial cancer risk, prevention, and treatment. J Clin Oncol. 2016 Dec;34(35):4225–30.

31. Crosbie EJ, Zwahlen M, Kitchener HC, Egger M, Renehan AG. Body mass index,

hormone replacement therapy, and endometrial cancer risk: A meta-analysis. Cancer Epidemiol Biomarkers Prev. 2010 Dec;19(12):3119–30.

32. Bhaskaran K, Douglas I, Forbes H, dos-Santos-Silva I, Leon DA, Smeeth L. Body-mass index and risk of 22 specific cancers: a population-based cohort study of 5·24 million UK adults. Lancet (London, England). 2014 Aug;384(9945):755–65.

33. Passarello K, Kurian S, Villanueva V. Endometrial Cancer : An Overview of Pathophysiology , Management , and care. Semin Oncol Nurs. 2019;35(2):157–65.

34. Lacey J V., Brinton LA, Lubin JH, Sherman ME, Schatzkin A, Schairer C. Endometrial carcinoma risks among menopausal estrogen plus progestin and unopposed estrogen users in a cohort of postmenopausal women. Cancer Epidemiol Biomarkers Prev. 2005;14(7):1724–31.

35. Thiyagarajan DK, Jeanmonod R. Physiology, Menstrual Cycle. Treasure Island (FL): StatPearls Publishing; 2019.

36. Botha MH. Endometrial carcinoma: A South African perspective. South African J Gynaecol Oncol. 2009;1(1):16–20.

37. Jindal A. Pathophysiology of endometrial carcinoma. In: Current Concepts in Endometrial Cancer. Springer Singapore; 2017. p. 29–39.

38. Ramirez PT, Salvo G. Endometrial Cancer (Uterus cancer). Online. 2019.

39. Cymbaluk-Płoska A, Chudecka-Głaz A, Pius-Sadowska E, Sompolska-Rzechuła A,

Machaliński B, Menkiszak J. Circulating Serum Level of Visfatin in Patients with Endometrial Cancer. Biomed Res Int. 2018;2018.

40. Felix AS, Weissfeld JL, Pfeiffer RM, Modugno F, Black A, Hill LM, et al. Endometrial thickness and risk of breast and endometrial carcinomas in the prostate, lung, colorectal and ovarian cancer screening trial. Int J cancer. 2014 Feb;134(4):954–60.

41. Zhou Q, Singh SR, Devi Tina SS, Wena J, Yiying Z, Mariella MS. The Pathways in Endometrial Carcinogenesis and an Overview of its Histology, Grade and Stage. Ann Clin Lab Res. 2018;06(01).

42. Sherman ME. Theories of endometrial carcinogenesis: A multidisciplinary approach. Mod Pathol. 2000;13(3):295–308.

43. PDQ Screening and Prevention Editorial Board. Endometrial Cancer Screening (PDQ®): Health Professional Version. PDQ Cancer Information Summaries. 2002.

44. National Cancer Institute. Endometrial Cancer Treatment (PDQ®)—Health Professional Version. Natl Cancer Inst.

45. Morice P, Leary A, Creutzberg C, Abu-Rustum N, Darai E. Endometrial cancer. Lancet. 2016;387(10023):1094–108.

46. Vidal F, Rafii A. Lymph Node Assessment in Endometrial Cancer: Towards Personalized Medicine. Obstet Gynecol Int. 2013;2013:1–8.

47. Charo LM, Plaxe SC. Recent advances in endometrial cancer: a review of key clinical

trials from 2015 to 2019. Vol. 8, F1000Research. F1000 Research Ltd; 2019.

48. Flores C, Mariscal C, Celis A, Balcázar NM, Meneses A, Mohar A, et al. Treatment Outcomes and Prognostic Factors in Mexican Patients with Endometrial Carcinoma with Emphasis on Patients Receiving Radiotherapy after Surgery: An Institutional Perspective. ISRN Oncol. 2012;2012:1–10.

49. Choi EC, Kim JH, Kim OB, Byun SJ, Park SG, Kwon SH. Postoperative radiotherapy for endometrial cancer. Radiat Oncol J. 2012;30(3):108–16.

50. Sunil RA, Bhavsar D, Shruthi MN, Kunikullaya US, Vyas RK, Parikh A, et al. Combined external beam radiotherapy and vaginal brachytherapy versus vaginal brachytherapy in stage I, intermediate- and high-risk cases of endometrium carcinoma. J Contemp Brachytherapy. 2018;10(2):105–14.

51. Zhang Y, Wang J. Controversies in the Management of Endometrial Carcinoma. Obstet Gynecol Int. 2010;

52. Wright JD, Fiorelli J, Kansler AL, Burke WM, Schiff PB, Cohen CJ, et al. Optimizing the management of stage II endometrial cancer: the role of radical hysterectomy and radiation. Am J Obstet Gynecol. 2009;200(4):419.e1-419e7.

53. Bestvina CM, Fleming GF. Chemotherapy for Endometrial Cancer in Adjuvant and Advanced Disease Settings. Oncologist. 2016 Oct;21(10):1250–9.

54. Leslie KK, Thiel KW, Goodheart MJ, De Geest K, Jia Y, Yang S. Endometrial Cancer. Obstet Gynecol Clin North Am. 2012;39(2):107–322.

55. Carlson MJ, Thiel KW, Leslie KK. Past, present, and future of hormonal therapy in recurrent endometrial cancer. Int J Womens Health. 2014 May;6 .(1):429–35.

56. Kokka F, Brockbank E, Oram D, Gallagher C, Bryant A. Hormonal therapy in advanced or recurrent endometrial cancer [Internet]. Vol. 2010, Cochrane Database of Systematic Reviews. John Wiley and Sons Ltd; 2010. p. 01–12. Available from: https://dx.doi.org/10.1002%2F14651858.CD007926.pub2

57. Hopkins J, Tanner E, Santin A, Tran A-Q, Gehrig P. Recent Advances in Endometrial Cancer. F1000 Fac Res. 2017;6(81).

58. Longoria TC, Eskander RN. Immunotherapy in endometrial cancer - an evolving therapeutic paradigm. Gynecol Oncol Res Pract. 2015 May;2(1):11.

59. Kalebi. A CF, Mwang'ombe.N, Narayanan.V. Kenya national cancer treatment protocols. Natl Cancer Control Progr. 2019;(July):93.

60. Uharcek P. Prognostic factors in endometrial carcinoma. Japan Soc Obstet Gynecol. 2008;34(5):776–83.

61. American Cancer Society. Endometrial Cancer Survival Rates, by Stage. Online. 2017.

62. Greven KM, Lanciano RM, Herbert SH, Hogan PE. Analysis of complications in patients with endometrial carcinoma receiving adjuvant irradiation. Int J Radiat Oncol Biol Phys. 1991;21(4):919–23.

63. Piovano E, Fuso L, Poma CB, Ferrero A, Perotto S, Tripodi E, et al. Complications after

the treatment of endometrial cancer: a prospective study using the French-Italian glossary. Int J Gynecol Cancer. 2014 Mar;24(3):418–26.

64. Dinkelspiel HE, Wright JD, Lewin SN, Herzog TJ. Contemporary Clinical Management of Endometrial Cancer. Obstet Gynecol Int. 2013;2013:1–11.

65. Lindqvist E, Wedin M, Fredrikson M, Kjølhede P. Lymphedema after treatment for endometrial cancer − A review of prevalence and risk factors. Eur J Obstet Gynecol Reprod Biol. 2017 Apr;211(201):112–21.

66. Arthritis Research UK. What are the possible complications of endometrial carcinoma? [Internet]. Mescape. 2018. Available from: https://www.medscape.com/answers/254083-116415/what-are-the-possible-complications-of-endometrial-carcinoma

67. United Nations Department of Economic and Social Affairs Population. World Mortality 2019 [Internet]. World Mortality 2019. United Nations; 2019. Available from: https://www.un.org/en/development/desa/population/publications/pdf/mortality/WMR2019/WMR2019_Highlights.pdf

68. Ministry of Health. National Guidelines for Cancer Managment in Kenya [Internet]. 2019. Available from: https://www.health.go.ke/wp-content/uploads/2019/09/National-treatment-Protocols-2019.pdf

69. Kenyatta National Hopital. KENYATTA NATIONA HOSPITAL STRATEGIC PLAN FOR 2013-2018. 2019; Available from: https://knh.or.ke/wp-content/uploads/2017/03/KNH_Strategic_Plan_2013-2018.pdf.pdf

70. Akech JEO. Demand for Emergency Caesarean Delivery at Kenyatta National Hospital: Free Maternal Health Care Program [Internet]. 2016. Available from: http://erepository.uonbi.ac.ke/handle/11295/100001

71. Yang X, Wang J. The Role of Metabolic Syndrome in Endometrial Cancer: A Review. Front Oncol. 2019 Aug;9.

72. Shaw E, Farris M, McNeil J, Friedenreich C. Obesity and Endometrial Cancer. In 2016. p. 107–36.

73. Hernandez VMV, Aguilar VMV. Endometrial Cancer; Clinical Aspects and Prognosis. Austin J Womens Heal. 2015;2(2):1016.

74. Burbos N, Musonda P, Giarenis I, Shiner AM, Giamougiannis P, Morris EP, et al. Predicting the risk of endometrial cancer in postmenopausal women presenting with vaginal bleeding: the Norwich DEFAB risk assessment tool. Br J Cancer. 2010 Apr;102(8):1201–6.

75. Buhtoiarova TN, Brenner CA, Singh M. Endometrial Carcinoma. Am J Clin Pathol. 2016 Jan;145(1):8–21.

APPENDICES

Appendix A: Verbal Consent Form

Title of Study: CLINICAL CHARACTERISTICS AND TREATMENT OUTCOMES OF PATIENTS WITH ENDOMETRIAL CANCER IN KENYATTA NATIONAL HOSPITAL, 2012 -2018

Principal Investigator: Dr Yoni Biko. **Institutional affiliation:** University of Nairobi

Introduction/Background:

I would like to tell you about a study being conducted by the above listed researchers. The purpose of this consent form is to give you the information you will need to help you decide whether or not to be a participant in the study. Feel free to ask any questions about the purpose of the research, what happens if you participate in the study, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions to your satisfaction, you may decide to be in the study or not. This process is called 'informed consent'. You should understand the general principles which apply to all participants in a medical research:

i. Your decision to participate is entirely voluntary
ii. You may withdraw from the study at any time without necessarily giving a reason for your withdrawal
iii. Refusal to participate in the research will not affect the services you are entitled to in this health facility or other facilities. .

May I continue? ***(YES / NO)***

This study has been approved by The Kenyatta National Hospital-University of Nairobi Ethics and Research Committee protocol No. _____

WAT IS THIS STUDY ABOUT

Globally, endometrial cancer (EMC) is among the commonest gynecological malignancies occurring in women. This study seeks to evaluate the clinical characteristics and treatment outcomes of patients managed for endometrial cancer in Kenyatta National Hospital (KNH), 2012 -2018.

WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH STUDY?

If you agree to participate in this study, the following things will happen:

- You will be interviewed by a trained interviewer via phone at your convenient time
- The interview will last approximately 5 - 15 minutes.
- The interview will cover topics such as; sociodemographic, health assessment history, risk factors for endometrial cancer, treatment and management of endometrial cancer, complications and outcomes.

RISKS, HARMS and DISCOMFORTS ASSOCIATED WITH THIS STUDY

Medical research has the potential to introduce psychological, social, emotional and physical risks. Effort should always be put in place to minimize the risks. One potential risk of being in the study is loss of privacy. We will keep everything you tell us as confidential as possible. We will use a code number to identify you in a password-protected computer database and will keep all of our paper records in a locked file cabinet. However, no system of protecting your confidentiality can be absolutely secure, so it is still possible that someone could find out you were in this study and could find out information about you.

Also, answering questions in the interview may be uncomfortable for you. If there are any questions you do not want to answer, you can skip them. You have the right to refuse the interview or any questions asked during the interview.

ARE THERE ANY BENEFITS BEING IN THIS STUDY?

There will be no immediate benefit to you. However, the information you provide will help us better understand risk factors, appropriate management approaches, and foreseeable complications for endometrial cancer. This information is a contribution to science and will greatly improve screening and future management of patients with endometrial cancer

WILL BEING IN THIS STUDY COST YOU ANYTHING?

This study involves extracting data from the patients file, therefore, no financial contribution is required from you or other involved study participants. The researcher will make the phone calls.

WILL YOU GET REFUND FOR ANY MONEY SPENT AS PART OF THIS STUDY?

No financial appreciation will be offered for participating in the study

WHAT IF YOU HAVE QUESTIONS IN FUTURE?

If you have further questions or concerns about participating in this study, please call or send a text message to the study staff at the number provided at the bottom of this page.

For more information about your rights as a research participant you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee: Telephone No. 2726300 Ext. 44102, Email: uonknh_erc@uonbi.ac.ke.

The study staff will pay you back for your charges to these numbers if the call is for study-

related communication.

WHAT ARE YOUR OTHER CHOICES?

Your decision to participate in research is voluntary. You are free to decline participation in the study and you can withdraw from the study at any time without injustice or loss of any benefits.

STATEMENT OF CONSENT

Participant's statement

The information in this consent form has been read to me. I have had my questions answered in a language that I understand. The risks and benefits have been explained to me. I understand that my participation in this study is voluntary and that I may choose to withdraw any time. I freely agree toparticipate in this research study. I understand that all efforts will be made to keep information regarding my personal identity confidential.

By agreeing to take part in this study, I have not given up any of the legal rights that I have as a participant in a research study.

	Yes	**No**
I agree to participate in this research study:		
I agree to provide contact information for follow-up:		

Participant Name: _____Date_____

Researcher's statement

I, _____, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has willingly and freely given his/her consent.

Researcher's Name:_____

Signature:_____**Date**_____

Role in the study:*[i.e. study staff who explained informed consent form.]*

For more information contact:***Dr. Yoni Biko***at***0722510715***from***08:00 am*** *to****6:00 pm***

Appendix B: Data Collection Form

Title: Clinical Characteristics and Treatment Outcomes of Patients with Endometrial Cancer in Kenyatta National Hospital, 2012 -2018

The study tool has four sections (sections A, B, C &D). Each section has specific instructions on what is expected and how the data will be abstracted from the patient file. Inconsistencies noted or missing information will be clarified with the patient using the contact provided in the file.

Section A: Socio-Demographic Data

Abstract the information from the files as guided by the demographic prompts below. Peruse the file to ensure that information is the most current and accurate.

a. Age at diagnosis (in years) ……..
b. Year of birth ……
c. Ethnicity ……
d. Education Level
    i. *No formal education { }*
    ii. *Primary Level { }*
    iii. *Secondary level { }*
    iv. *College/University { }*
e. Occupation
    i. Student { }
    ii. Casual Labourer { }
    iii. Self-employed { }

iv. *Formal Employment { }*

v. *Unemployed { }*

vi. *Other*

f. Marital status

i. *Never married ( )*

ii. *Married ( )*

iii. *Separated ( )*

iv. *Divorced*

v. *Widowed ( )*

g. County of residence ……..

Section B: Reproductive History

h. Menarche …….

i. Menstrual length …….days,

j. Regularity of menses

i. *Regular [ ]*

ii. *Irregular [ ]*

Section C: Risk Factors

k. History of smoking

i. *Never Smoked [ ]*

ii. *Used to [ ]*

iii. *Regular smoker [ ]*

l. History of alcohol intake

i. *Never taken alcohol [ ]*

ii. *Used to [ ]*

iii. *Regularly take alcohol [ ]*

m. Height in Metres.....

n. Weight in Kilograms……

o. Body Mass Index …….

p. Usual adult weight……

q. History of the pregnancy (*fill in the information in the table below***)**

Birth Order	**Year of Birth**	**Gestation at delivery**	**Breastfeeding done (Yes or No)**	**Duration of Breastfeeding**
1.				
2.				
3.				
4.				
5.				
6.				
7.				

r. Did the patient have a history of any of these conditions at diagnosis? (*tick all that applies***)**

Condition	**Family History**			**Personal History**	
	YES	**NO**	**Not Sure**	**Yes**	**No**
Diabetes					
Chronic hypertension					
Colorectal cancer					
Ovarian cancer					
Breast cancer					
Endometriosis					

Condition	Family History			Personal History	
	YES	**NO**	**Not Sure**	**Yes**	**No**
HIV					
Others, state_____					

s. What family planning methods has the patient ever used? (*tick all that applies***)**

Family Planning Method	YES	Cumulative Duration of use in Months	NO	Not Sure
Progesterone Only Pills				
Combine oral contraceptives				
Copper T coil				
Depo-Provera				
Implants				
Tubal ligation				
Mirena (Hormonal IUD)				
None of the above				
Others …….				

Section B: Endometrial Cancer (EMC) Diagnosis Characteristics

a. What were the main clinical presentations with the patient at the time of diagnosis?

Clinical presentation	Yes	No	No Information
Irregular menstrual bleeding			
Bleeding between periods			
Vaginal bleeding after menopause			
Abdominal pain			
Pelvic pain			
Abdominal mass			
Dyspareunia			
Persistent bloating			
Feeling full with occasionally small amount of food			
Others_____			

*b. Fill in the details as can be abstracted from the file. In case the details are missing indicate **N/A***

Age at EMC diagnosis	EMC Grade at diagnosis	EMC Staging at diagnosis	Name of the hospital where	Name of the hospital where confirmed

	1	2	3	I	II	III	IV	Diagnosed	(histologically)

c. Date when specimen as collected ……..

d. Histologic type ……..

Section C: Management/Treatment (tick all that applies)

What EMC management approach(es) did the patient receive in each of the years of care? Where more than one approaches in a year, indicate the first with one tick (√) second option with two ticks, (√√) and third with three in that order (√√√)

Management/treatment	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Surgery (Indicate type)					
Adjuvant therapy					
Radiation therapy					
Chemotherapy					
Hormonal therapy					
Novel therapeutic techniques					
Other modalities,					

Section D: EMC Patient Outcomes

a. Did the patient recover from EMC? Yes. ….. No …...

b. If yes, after how many years of treatment? …….

c. If no above (*question a*), is the patient still on treatment? Yes ….. No ……

d. Did the condition recur?

e. How long did the patient survive after the diagnosis? ……

f. The exact cause of death?

Appendix C: Approval from KNH-UON Ethics and research Committee

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/344

6th October 2020

Dr. Yoni Biko
Reg. No.H58/6973/2017
Dept. of Obstetrics and Gynaecology
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Biko

RESEARCH PROPOSAL – CLINICAL CHARACTERISTICS AND TREATMENT OUTCOMES OF PATIENTS WITH ENDOMETRIAL CANCER IN KENYATTA NATIONAL HOSPITAL, 2012-2018 (P344/06/2020)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 6th October 2020 – 5th October 2021.

This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
g. Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

Appendix D: KNH Records department registration certificate

KNH/R&P/FORM/01

KENYATTA NATIONAL HOSPITAL
P.O. Box 20723-00202 Nairobi

Tel.: 2726300/2726450/2726565
Research & Programs: Ext. 44705
Fax: 2725272
Email: knhresearch@gmail.com

Study Registration Certificate

1. Name of the Principal Investigator/Researcher
   Dr. YONI STEVE BIKO.
2. Email address: yonibiko@gmail.com Tel No. 0722510715
3. Contact person (if different from PI).....
4. Email address: ..... Tel No. .....
5. Study Title
   CLINICAL CHARACTERISTICS AND TREATMENT OUTCOMES OF PATIENTS WITH ENDOMETRIAL CANCER IN KENYATTA NATIONAL HOSPITAL 2012 - 2018
6. Department where the study will be conducted RECORDS DEPARTMENT. Obs Gyn
   (Please attach copy of Abstract)
7. Endorsed by Research Coordinator of the KNH Department where the study will be conducted.
   Name: DR. IKOL KOUNGO Signature ..... Date 15/10/2020
8. Endorsed by KNH Head of Department where study will be conducted.
   Name: [illegible] Signature ..... Date 15/10/2020
9. KNH UoN Ethics Research Committee approved study number P344/06/2020
   (Please attach copy of ERC approval)
10. I YONI STEVE BIKO commit to submit a report of my study findings to the Department where the study will be conducted and to the Department of Research and Programs.
    Signature..... Date 15/10/2020.
11. Study Registration number (Dept/Number/Year) Obs Gyn /1402/2020
    (To be completed by Research and Programs Department)
12. Research and Program Stamp

KENYATTA NATIONAL HOSPITAL * Research & Programs * P.O. Box 20723-00202 NAIROBI
16 OCT 2020

All studies conducted at Kenyatta National Hospital **must** be registered with the Department of Research and Programs and investigators **must commit** to share results with the hospital.

Version 2: August, 2014