MANAGEMENT AND SURVIVAL OF INPATIENTS WITH STAGE IIIB CERVICAL CANCER WITH HYDRONEPHROSIS ADMITTED AT KENYATTA NATIONAL HOSPITAL, 2012-2017

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DECLARATION

This project dissertation is my original work and references have been made for work done by others.

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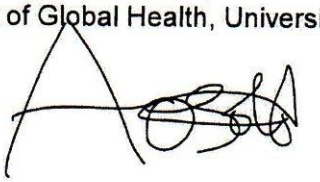
Signature  Date 2.11.21

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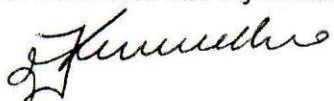
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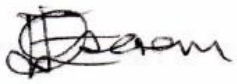
This research was carried out in the Department of Obstetrics and Gynecology, School of Medicine, College of Health sciences, University of Nairobi. It has not been presented in any other University for award of a degree.

Signature  Date 03/11/21

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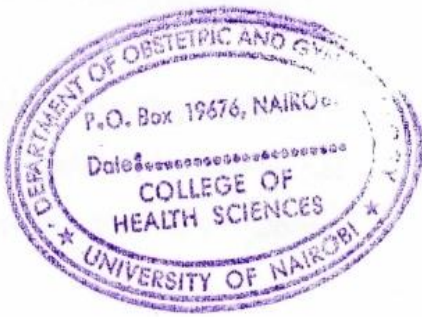

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DEDICATION

To my husband Tim Alala, and to my children Abby, Tessy, Teddy and Andy

Thank you for your endless love, sacrifices, prayers, and support

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LIST OF ABBREVIATIONS

AKI	Acute kidney injury
CT	Computerized tomography
DJ	Double J
FIGO	International Federation of Gynecology and Obstetrics
HIV	Human Immunodeficiency Virus
HPV	Human Papillomavirus
ICD	International Classification of Diseases
KNH	Kenyatta National Hospital
MRI	Magnetic Resonance Imaging
NHIF	National Health Insurance Fund
SFU	Society of Fetal Urology

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ABSTRACT

Introduction: In FIGO stage IIIB cervical cancer, the carcinoma involves the lower third of the vagina with extension to the pelvic wall and/or hydronephrosis or non-functioning kidney. Patients with hydronephrosis have worse morbidity compared to those with extension to pelvic wall only. Morbidity among patients with hydronephrosis include acute renal injury and ultimate poor survival. Outcomes for patients with FIGO stage IIIB cervical cancer has not been evaluated in Kenyatta National Hospital. This is particularly important, because majority of mortalities in cervical cancer patients is due to renal complications.

Broad Objective: To evaluate the management and survival of inpatient FIGO stage IIIB cervical cancer patients with hydronephrosis admitted at KNH between 2012 and 2017

Methodology
Study design: Retrospective descriptive cohort
Study site and setting: Kenyatta National Hospital
Study population: Cervical cancer patients with FIGO stage IIIB with hydronephrosis
Sample size: 448
Data collection: Descriptive variables, variables on management of hydronephrosis, date and time of death were collected. Data was captured electronically into the REDcap software. ***Data analysis:*** Data with descriptive statistics were summarized. Age was presented as means (SD), while categorical data was presented in proportions. Survival was presented as median (IQR) and Kaplan Meier curves were used to determine 2- and 5-year survivals.

Results: The overall mean (SD) age was 49.1(11.8) years. A total of 252 patients had their histology report in the file, out of these, 89% (224/448) were squamous cell carcinoma. The median (IQR) survival in months was 1.4 (0.4-5.4). Most patients (55%) had their cancer treatment written as radiotherapy given, without details on if concurrent chemotherapy was given, type of radiation, radiation dose or number of cycles. Most (75%) patients presented with bilateral hydronephrosis, over 80% had ungraded hydronephrosis, and over 60% had no decompression for their hydronephrosis. Patients who received decompression for hydronephrosis had better 2 and 5-year survival compared to those who did not, though by a few days, log rank test p= <0.001.

Conclusion: Squamous cell carcinoma is the commonest histologic type in inpatient FIGO stage IIIB cervical cancer patients with hydronephrosis admitted and managed at KNH between 2012 and 2017. Radiotherapy treatment was not clearly indicated in most, had bilateral hydronephrosis and decompression was not offered for many patients. The overall median survival in months (IQR) was 1.4(0.4-5.4). Though patients who received decompression for hydronephrosis had better survival, this is only by a few days. Decompression of hydronephrosis should not delay definitive chemoradiation therapy.

CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW

INTRODUCTION

Every year in Africa, 119,284 women are diagnosed with cervical cancer and 81,687 (68%) die from it. It ranks as the second most frequent cancer among women in the continent, however in Eastern Africa it ranks first. Eastern Africa bears the greatest burden of total cases (44%) and deaths (45%) in the region. In Kenya there are 5,250 new cases and Age−standardized cervical cancer incidence and mortality rate in Kenya is 33.8 and 22.8 per 100, 000 women respectively, which is lower than the overall Eastern African rate of 40.1 and 30 respectively (1). The regional specific statistics given are not stratified into the specific International Federation of Gynecology and Obstetrics (FIGO) stages (box 1) (2).

In a Kenyan study among patients with advanced cervical cancer undergoing radiotherapy in a Kenyatta National Hospital (KNH), the mean age (range) at presentation 49 years (21–94), the common histologic types were squamous cell carcinoma (90%), and adenocarcinoma (6%). Squamous cell carcinoma tumor grades were well differentiated, moderately differentiated, and poorly differentiated in 21%, 39% and 32% respectively. At diagnosis the frequency of per FIGO stage was stage IA (2.2%), IB (7.3%), IIA (8.5%), IIB (29.9%), IIIA (16.1%), IIIB (25.6%), IVA (7.3%) and IVB (3.1%) (3).

In FIGO stage IIIB, the carcinoma involves the lower third of the vagina with extension to the pelvic wall and/or hydronephrosis or non-functioning kidney(2). Patients with hydronephrosis have worse morbidity that include acute renal injury and ultimate poor survival compared to those patients with extension to pelvic side wall only (4, 5).

Hydronephrosis can lead to renal injury ± uremia due to associated obstructive uropathy. Obstruction is due to external compression or malignant involvement of lower ureters. Uremia is the most common cause of death in cervical cancer patients(6).

Therapies available to patients with stage IIIB hydronephrosis are relieve of urinary obstruction, dialysis, chemotherapy, and radiotherapy. Renal malfunctions are usually first addressed by relieving the obstruction or dialysis followed by chemotherapy and radiotherapy; this leads to a delay in offering the definitive cancer treatment (5-9). This delay can lead to progression of the cancer and a further delay in resolving the renal malfunctions; cancer specific treatment achieves tumor size reduction relieving the ureteric obstruction. Secondly, with renal impairment patients are ineligible for chemoradiation with cisplatin, rendering their treatment suboptimal.

In an American study, the progression-free survival at 5 years was 35% in in stage IIIB patients with both hydronephrosis and tumor fixed to pelvic side wall, 43% in stage IIIB patients with tumor fixed to the pelvic side wall only and 23% in stage IIIB patients with hydronephrosis only (4).

There are no studies in Kenya and the African region that have outcomes and survival for FIGO stage IIIB patients with hydronephrosis, who clearly have a different disease morbidity compared to those with pelvic extension alone. The results from the study will be used in KNH, to understand management of patient with FIGO stage IIIB cervical cancer with hydronephrosis. This will form baseline data for further studies on

this topic. Outcomes for patients with FIGO stage IIIB cervical cancer has not been evaluated in Kenyatta National Hospital. This is particularly important, because majority of mortalities in cervical cancer patients is due to renal complications. Results from this study will help understand the care we give to these patients, and how to optimize their outcomes.

LITERATURE REVIEW

Human papillomavirus (HPV) is a necessary cause of cervical cancer, but it is not a sufficient cause. Well studied and documented cofactors play a role for its progression from HPV infection to invasive cancer. The cofactors include tobacco smoking, high parity, long-term hormonal contraceptive use, early menarche and co-infection with Human Immunodeficiency Virus (HIV). Other probable cofactors are chlamydia trachomatis, herpes simplex virus type-2, and other non-HIV related immunosuppression like chronic steroid use (1). HIV infection leads to an increased risk of cervical cancer and is associated with a more rapid aggressive disease (10). In Kenya the HIV prevalence among women is 5.2%, less than 4% of females smoke tobacco, total fertility rate is 3.4 live births, hormonal contraceptive use is about 34%, (1, 11, 12).

Most patients in Africa present with late-stage cervical cancer, for instance in Morocco (55%), Uganda (66%) and Tanzania (64%) of patients present with advanced cancer (13-15). In Kenya, at the time of diagnosis the majority (80%) of patients present with stage FIGO IIB disease or above (3, 16). Factors associated with late presentation are lack of previous cervical cancer screening, low socio-economic status, not married, lower degree of education, being elderly, not covered by health insurance, of African

ethnicity, living in a rural area, HIV infection, and high parity (15, 17-19). Overall, late stage presentation is associated with lower survival rates (19).

Box 1 shows the FIGO staging for cervical cancer(2). This research will focus on cervical cancer stage IIIB. In FIGO stage III the carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or non-functioning kidney and/or involves pelvic and/or paraaortic lymph nodes. It is sub-classified to: a) stage IIIA, the carcinoma involves the lower third of the vagina, with no extension to the pelvic wall, b) stage IIIB, the carcinoma involves the lower third of the vagina, with extension to the pelvic wall with hydronephrosis or non-functioning kidney and c) stage IIIC, the carcinoma involves the lower third of the vagina, with involvement of pelvic and/or paraaortic lymph nodes (2).

Box 1 FIGO staging of carcinoma of the cervix uteri (2018).

Stage I:
The carcinoma is strictly confined to the cervix uteri (extension to the corpus should be disregarded)

- **IA** Invasive carcinoma that can be diagnosed only by microscopy, with maximum depth of invasion <5 mm[a]
  - **IA1** Measured stromal invasion <3 mm in depth
  - **IA2** Measured stromal invasion ≥3 mm and <5 mm in depth
- **IB** Invasive carcinoma with measured deepest invasion ≥5 mm (greater than stage IA), lesion limited to the cervix uteri[b]
  - **IB1** Invasive carcinoma ≥5 mm depth of stromal invasion and <2 cm in greatest dimension
  - **IB2** Invasive carcinoma ≥2 cm and <4 cm in greatest dimension
  - **IB3** Invasive carcinoma ≥4 cm in greatest dimension

Stage II:
The carcinoma invades beyond the uterus, but has not extended onto the lower third of the vagina or to the pelvic wall

- **IIA** Involvement limited to the upper two-thirds of the vagina without parametrial involvement
  - **IIA1** Invasive carcinoma <4 cm in greatest dimension
  - **IIA2** Invasive carcinoma ≥4 cm in greatest dimension
- **IIB** With parametrial involvement but not up to the pelvic wall

Stage III:
The carcinoma involves the lower third of the vagina and/or extends to the pelvic wall and/or causes hydronephrosis or non-functioning kidney and/or involves pelvic and/or paraaortic lymph nodes[c]

- **IIIA** Carcinoma involves the lower third of the vagina, with no extension to the pelvic wall
- **IIIB** Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney (unless known to be due to another cause)
- **IIIC** Involvement of pelvic and/or paraaortic lymph nodes, irrespective of tumor size and extent (with r and p notations)[c]
  - **IIIC1** Pelvic lymph node metastasis only
  - **IIIC2** Paraaortic lymph node metastasis

Stage IV:
The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. A bullous edema, as such, does not permit a case to be allotted to stage IV

- **IVA** Spread of the growth to adjacent organs
- **IVB** Spread to distant organs

[a]Imaging and pathology can be used, when available, to supplement clinical findings with respect to tumor size and extent, in all stages.
[b]The involvement of vascular/lymphatic spaces does not change the staging. The lateral extent of the lesion is no longer considered.
[c]Adding notation of r (imaging) and p (pathology) to indicate the findings that are used to allocate the case to stage IIIC. For example, if imaging indicates pelvic lymph node metastasis, the stage allocation would be stage IIIC1r and, if confirmed by pathological findings, it would be Stage IIIc1p. The type of imaging modality or pathology technique used should always be documented. When in doubt, the lower staging should be assigned.

Adopted from: Bhatla N, Berek JS, Cuello Fredes M, Denny LA, Grenman S, Karunaratne K, et al. Revised FIGO staging for carcinoma of the cervix uteri. International Journal of Gynecology & Obstetrics. 2019;145(1):129-35.

FIGO stage IIIB has two groups of patients, those with a) tumor fixation to the pelvic side wall and/or b) hydronephrosis due to tumor. The two sub-groups also have different treatment outcomes and survival. Those with hydronephrosis have a poor progression free survival (4, 5).

Hydronephrosis develops when a blockage in the renal collecting system leads to distention of the renal calyces. In cervical cancer it can occur from the tumor or lymph

node compression of the ureters (5, 20). Urological complications associated with stage III B include urinary tract infections, vesicovaginal fistulas, ureter obstructions, hydronephrosis, and renal failure, and any of these can increase the morbidity and mortality of advanced stage cervical cancer patients (4, 5, 8)

Management of patients with stage IIIB cervical cancer include relieve of urinary obstruction, dialysis, chemotherapy, and radiotherapy. Renal malfunctions should first be addressed by relieving the obstruction or dialysis followed be chemotherapy and radiotherapy (5-9).

Almost all patients with bilateral hydronephrosis develop renal injury compared to those with unilateral hydronephrosis (5, 7, 8). Those with bilateral obstruction require immediate decompression of the kidney (21). If the obstruction is not decompressed, then the patient will progressively end up with uremia, water-electrolyte abnormalities and urinary infections, reduced consciousness and finally death (22, 23) .

Usually, obstruction is relieved with urinary diversions by either retrograde double-J ureteral stenting, percutaneous nephrostomy or open drainage of kidney(24, 25). Currently, retrograde double-J ureteral stenting and ultrasound guided percutaneous nephrostomy tube insertion are the most widely used techniques for relieving obstruction of the urinary tract obstruction (25, 26). Either method is associated with a number of complications. retrograde double-J ureteral stenting is associated with sepsis, irritable bladder, high failure rate and forgotten stents (27). Percutaneous nephrostomy is associated with bleeding, sepsis, tube blockage, dislodgement and extra care of external urine-collecting bag (23, 24, 26-28). Despite individual

complications, overall, ultrasound guided percutaneous nephrostomy is safe, quick and a better method of temporary urinary diversion compared to double J stenting for management of obstructive uropathy. Percutaneous nephrostomy is also preferred for drainage of hydronephrosis and ureteric obstruction due to malignant disease of pelvic origin (28). If obstruction is relieved early, acute kidney injury (AKI) might be prevented with an improvement in overall morbidity and mortality(29).

Hydronephrosis is commonly divided into four grades (1 to 4) by the society of Fetal Urology (SFU). Diagnosis is made by either ultrasound, computerized tomography (CT) scan or Magnetic resonance imaging (MRI) or a combination of any of the modalities. Box 2, outlines the severity classification and grading for hydronephrosis(30).

Box 2: Grading for hydronephrosis

Classification	Grade	Description
Normal	0	No dilatation
Mild	1	Dilatation of the renal pelvis without dilatation of the calices
	2	Dilatation of the renal pelvis and calices, that become convex; no signs of cortical thinning
Moderate	3	Presence of cortical thinning
Severe	4	Massive dilation of the real pelvis and calices, severe cortical thinning

Hydronephrosis in stage III B patients also has a strong relationship with survival, with those with bilateral hydronephrosis having a worse prognosis compared to those with unilateral hydronephrosis (9, 31).

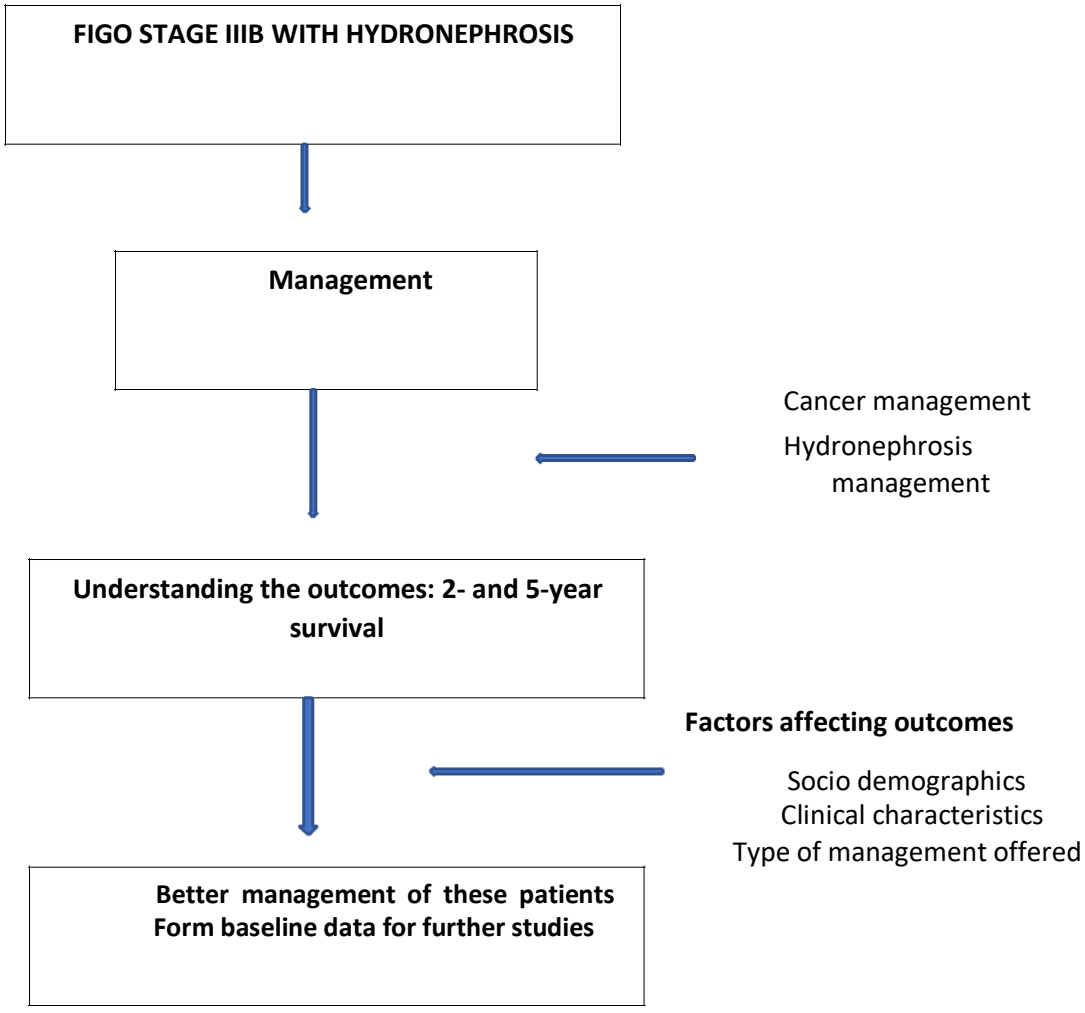
In an American study, the progression-free survival at 5 years was 35% in in stage IIIB patients with both hydronephrosis and tumor fixed to pelvic side wall, and 43% in stage IIIB patients with tumor fixed to the pelvic side wall only (4). There are no studies in Kenya and the African region that have stratified outcomes and survival for the two

groups in FIGO stage IIIB. In KNH, the overall median survival of patients undergoing radiotherapy is 15 months. The FIGO stage stratified median survival in stage I (21 months), II (18 months), III (15 months), and IV (11months) (3).

CONCEPTUAL FRAMEWORK NARRATIVE

Outcomes of cervical cancer FIGO stage IIIB with hydronephrosis depend on the management offered for the cancer and the hydronephrosis. Patient sociodemographic and clinical characteristics also affect outcome. In this study the outcome of interest is the 2-and 5-year survival. Understanding this interaction will help better management for these patients and will form baseline data for future studies.

CONCEPTUAL FRAMEWORK SCHEMA



JUSTIFICATION

In KNH 26% of all cervical cancer patients present in FIGO stage IIIB, with squamous cell carcinoma being the most frequent histologic type followed by adenocarcinoma. In FIGO stage IIIB, the carcinoma involves the lower third of the vagina with extension to the pelvic wall and/or hydronephrosis or non-functioning kidney. Patients with hydronephrosis have a worse morbidity that include acute renal injury, uremia and poor survival. Uremia is the most common cause of death in cervical cancer patients.

In KNH, chemoradiation therapy for FIGO stage IIIB with hydronephrosis is given as outpatient treatment. Only patients who have superimposed acute conditions like renal failure or anemia are admitted for optimization. Specifically, for FIGO stage IIIB with hydronephrosis are usually admitted for decompression before chemoradiation.

There are no studies in Kenya and the African region that have outcomes and survival for FIGO stage IIIB patients with hydronephrosis, who clearly have a different disease morbidity compared to those with pelvic extension alone. The results from the study will be used in KNH, to understand management of patient with FIGO stage IIIB cervical cancer with hydronephrosis. This will form baseline data for further studies on this topic. This study seeks to determine the management and survival of stage IIIB cervical cancer women with hydronephrosis admitted at KNH, between 2012 and 2017.

RESEARCH QUESTION

What is the management and survival of inpatient FIGO stage IIIB cervical cancer women with hydronephrosis admitted at KNH, between 2012 and 2017?

BROAD OBJECTIVE

To evaluate the management and survival of inpatient FIGO stage IIIB cervical cancer women with hydronephrosis admitted at KNH between 2012 and 2017

SPECIFIC OBJECTIVES

Among inpatient women with FIGO stage IIIB cervical cancer with hydronephrosis admitted in KNH, 2012-2017 to determine the:

1. Cervical cancer histopathology and treatment modality offered
2. Management of hydronephrosis
3. Survival

CHAPTER 2: METHODOLOGY

STUDY DESIGN

This was a retrospective descriptive cohort. Routine care records of women who meet the eligibility criteria were reviewed. The cohort was made up of inpatient FIGO stage IIIB cervical cancer patients with hydronephrosis admitted in KNH between 2012 and 2017. This study design was appropriate to answer the objectives of the study because a descriptive cohort study allowed for follow up of patients through the continuum of care. A retrospective design allowed follow up of patients for at least 2 years for all patients and 5 years for some patients.

STUDY SITE AND SETTING

The study was carried out in KNH, Nairobi Kenya. KNH is the largest referral hospital in Kenya. It also serves as the teaching hospital of University of Nairobi and Kenya Medical Training College. Its catchment area is drawn from all over the country and the region. The whole hospital has a bed capacity of 2,500 patients, though largely its bed occupancy is mostly double.

Patients diagnosed with advanced cancer of the cervix are managed in the Department of Obstetrics and Gynecology in the gynecologic oncology outpatient clinic 18, theatres, gynecologic oncology wards 1B and 1D. Other departments that actively manage these patients are the Pathology Department, Interventional Radiology, and the Radiotherapy Department.

Examination under anesthesia for staging and biopsy is carried out for patients who have not been staged in KNH theatres. Training has been done to standardize staging

and biopsy of patients in KNH. For patients who are referred and have already been staged and biopsied, in peripheral facilities, the clinician repeats the staging without anesthesia to confirm the stage before proceeding with care.

In the outpatient clinic, management plans for new patients are made and reviews for patients in care is carried out. Patients with acute conditions, those requiring chemotherapy or salvage radiotherapy are admitted and managed in the wards. Acute conditions that require admission include renal failure, anemia, deep venous thrombosis, acute infections and per vaginal bleeding. Specifically for FIGO stage IIIB patients with hydronephrosis, chemoradiation is given as an outpatient treatment unless there is renal compromise, in which case they are admitted until renal functions are optimized.

Chemoradiation with cisplatin is the standard definitive treatment for FIGO stage IIIB, except of patients who are ineligible for chemotherapy due to renal impairment. Both external beam radiotherapy (EBRT) and brachytherapy are offered in the Radiotherapy unit. Once patient's complete radiotherapy treatment they are referred to the gynecologic oncology for follow-up. Follow-up is lifelong for all patients with reproductive tract cancers who are managed in the gynecologic oncology unit. Depending on the condition follow up is once every 2 weeks to 6 months.

Standard of care for patients with FIGO stage IIIB with hydronephrosis and renal impairment is decompression by either a nephrostomy tube or a DJ stent. This commenced in 2008 in KNH. Usually, a nephrostomy tube is inserted temporarily, once the tumor is treated and reduction in size is appreciated, a DJ stent is inserted.

Some patients due to financial constraints may not have these procedures performed in a timely manner. Box 3, summaries the cost of nephrostomy tube and DJ stent insertion in KNH. The National Health Insurance Fund (NHIF) can only co-pay up to a maximum of 40,000.

Box 3: cost of nephrostomy tube and DJ stent in Kenyatta National Hospital		
#	**Procedure**	**Cost in Kenyan shillings**
1.	Unilateral nephrostomy tube	52,000
2.	Bilateral nephrostomy tube	65,000
3.	Unilateral DJ stent	35,000
4.	Bilateral DJ stent	45,000

A multidisciplinary team approach is employed in care. Other auxiliary services that form part of the Gyn Oncology unit include Departments of General Surgery, Plastic Surgery, Urology, Urogynecology, Nutrition, Palliative Care and Psychosocial Support.

The staff compliment of the unit is comprised of one Gyn Oncologists, eight Gyn Oncology Fellows, Obstetrics and Gynecology residents and nurses.

The Records Department is integral to the care of cervical cancer patients. The KNH Records Department keeps a record of cancer patients admitted and managed as inpatients. Patients who are not admitted and are managed as outpatient, have their records kept manually in clinic registers. The ICD (International Classification of Diseases)-10 disease code is used. For cervical cancer, segregation by FIGO stage is not done, all the stages are pooled into disease code C53 (malignant neoplasms of cervix uteri), C53.1 (malignant neoplasms, exocervix) and C53.9 (malignant neoplasms, cervix uteri, unspecified). Patients who are managed in the Radiotherapy Department and not admitted, do not have their records captured in the Records

Department. The Radiotherapy Department keeps an independent records system that is different from the rest of the hospital. The two records systems are not linked.

STUDY POPULATION

Inpatient women with FIGO stage IIIB cervical cancer admitted in KNH between, 2012 and 2017

Inclusion criteria

1. Those with hydronephrosis

Exclusion criteria

1. Missing files
2. Where diagnosis is not explicit
3. Those with pelvic wall involvement only
4. Those with pelvic wall with node involvement

SAMPLE SIZE CALCULATION

The estimate used in sample size calculation is from a study done in KNH by Maranga I.O et.al. Among patients receiving radiotherapy in KNH, the proportion of those with FIGO stage IIIB was 26%(3). Even though it did not stratify for those with hydronephrosis, this is the closest estimate that will mirror the number of those with hydronephrosis.

Using a conservative incidence rate of 26% the sample size was determined by fishers' formula as follows:

$$n = \frac{Z^2 Pq}{d^2}$$

Where,

n =desired samples size

Z = standard normal deviation, which corresponds to the 95% Confidence Level (1.96)

p =proportion in the target population that is estimated to be to have stage IIIB. The incidence is 26%.

q =(1- p) = 1 – 0.26.

d = degree of accuracy desired set at 0.05 (±5%)

Hence;

$$n = \frac{1.96^2 \times 0.26 \times 0.74}{(0.05)^2} = 296$$

Using the 2-year loss to follow-up rate of 41% reported by Maranga et.al (3), the effective sample size accounting for loss to follow up is 414. We were able to collect data from 448 files.

SAMPLING PROCEDURE

Case records with diagnostic code for cervical cancer as outlined in study site and setting were retrieved. Using the KNH information management system, IP numbers were identified for all records meeting this diagnostic criterial for the period 2012 - 2017 for retrieval.

Retrieval of patient files started with screening all records that met the eligibility criteria as described in study population. Based on the number of files that met these criteria, a proportion of files were randomly selected until our estimated sample was arrived.

DATA VARIABLES

Box 4 outlines the data variables.

Box 6: data variables

Specific Objectives	Dependent variable	Sources of data
1. Descriptive variables	**Socio-demographic** Age Marital status (married, not married) Religion Occupation Education level NHIF registered **Clinical** Parity Family planning Smoking HIV status o Lowest recorded CD4 count o Lowest recorded viral load Comorbidities o Diabetes o Hypertension o DVT o Anemia Time to events FIGO stage Histological type o Squamous cell carcinoma o Adenocarcinoma o Adenosquamous carcinoma o Others –specify Tumor grade o Well differentiated o Moderately differentiated o Poorly differentiated o Others	Patient file record
2. Determine the management of hydronephrosis	**Diagnosis of hydronephrosis** Date of diagnosis of hydronephrosis Mode of diagnosis o Computerized tomography (CT) alone o MRI alone o Ultrasound scan alone o Both CT and ultrasound scan o CT/MRI/US o Other	

		Hydronephrosis symmetry status ○ Bilateral ○ Unilateral Grade of hydronephrosis ○ Mild ○ Moderate **Renal injury** Highest recorded ○ Urea ○ Creatinine ○ Potassium **Therapy modalities** Relieve of hydronephrosis ○ Nephrostomy tube alone ○ DJ stent alone ○ Nephrostomy tube followed by DJ stent ○ DJ stent followed by nephrostomy tube ○ No relieve Dialysis ○ Yes ○ No Cumulative cancer therapy ○ External beam radiotherapy (EBRT) alone ○ External boost ○ EBRT + Brachytherapy ○ EBRT + chemotherapy ○ Brachytherapy alone ○ Brachytherapy + chemotherapy ○ Chemotherapy alone ○ Other ○ No cancer treatment
3.	Determine the 5-year survival of those with hydronephrosis	Date of death Time to death in months Mean/median follow up time Date of last follow up at KNH If dead, date of death

call

DATA COLLECTION AND MANAGEMENT

A data abstraction tool (appendix 1) was created using the variables in box 4. A soft version of the data abstraction tool was created using, an electronic data capture software called Research Electronic Data Capture (REDcap). Research assistants were trained by the Principal Investigator on data abstraction from patient files.

To reduce missing data for survival analysis, patients whose follow-up status was not known were called using the number provided to records department during the initial registration at Kenyatta National Hospital. Date of last follow-up at Kenyatta National hospital and or dead of death are the only variables collected during the phone calls.

Data was abstracted directly into the REDcap software. At the end of data collection, data was exported to an excel database.

QUALITY ASSURANCE

The research assistants were nurses who work at the KNH Research and Projects Office. They were all trained and certified in good clinical practice.

The Data abstraction tool was piloted together with the REDcap software which was used for electronic data capture. The REDcap software has in-built range and consistency checks which were enforced in the database.

DATA ANALYSIS

Data was exported from Excel database to Stata software for analysis. Only de-identified data was analyzed. Description of data analysis is per objective.

Descriptive characteristics: Data with descriptive statistics was summarized. Age was presented as means (SD). Parity, and survival in months, was presented as median (IQR). Categorical data was presented in proportions.

Determining cervical cancer histopathology and treatment modality offered: Data on histological types and cancer treatment offered was categorized and presented in proportions.

Determining the management of hydronephrosis: Data on mode of diagnosis, type of hydronephrosis, grade of hydronephrosis, renal injury caused and type of treatment of hydronephrosis was categorized and presented in proportions.

Determining the 2 and 5-year survival: Sub-analysis was carried out to determine the 2 and 5-year survival of those who received decompression for hydronephrosis versus those who did not receive decompression. During analysis, 44% (196/448) of the total sample collected, had histology reported in the file notes, but no histology report in the file. A sensitivity analysis was carried out to compare 2 and 5-year survival of those with histology report available in the file versus those with just histology written in file without the histology report. Kaplan Meier curves was used to determine 2- and 5-year survivals. Patients who were alive or lost to follow up were censored in the survival analysis.

RESEARCH ETHICS

This study was submitted to the Kenyatta National Hospital/ University of Nairobi Ethics and Research Committee for approval. The study commenced after approval was given. Permission to carry out the study was sought from KNH. This study was considered of minimum risk due to its retrospective nature. No patient identifiers were collected. The data and results were kept confidential.

Verbal consent for the phone calls were sought (appendix 2). Only information on last follow-up clinic and or date of death was collected. The consent was sought in a polite and empathetic language.

STUDY LIMITATIONS

The following are study limitations for this study:

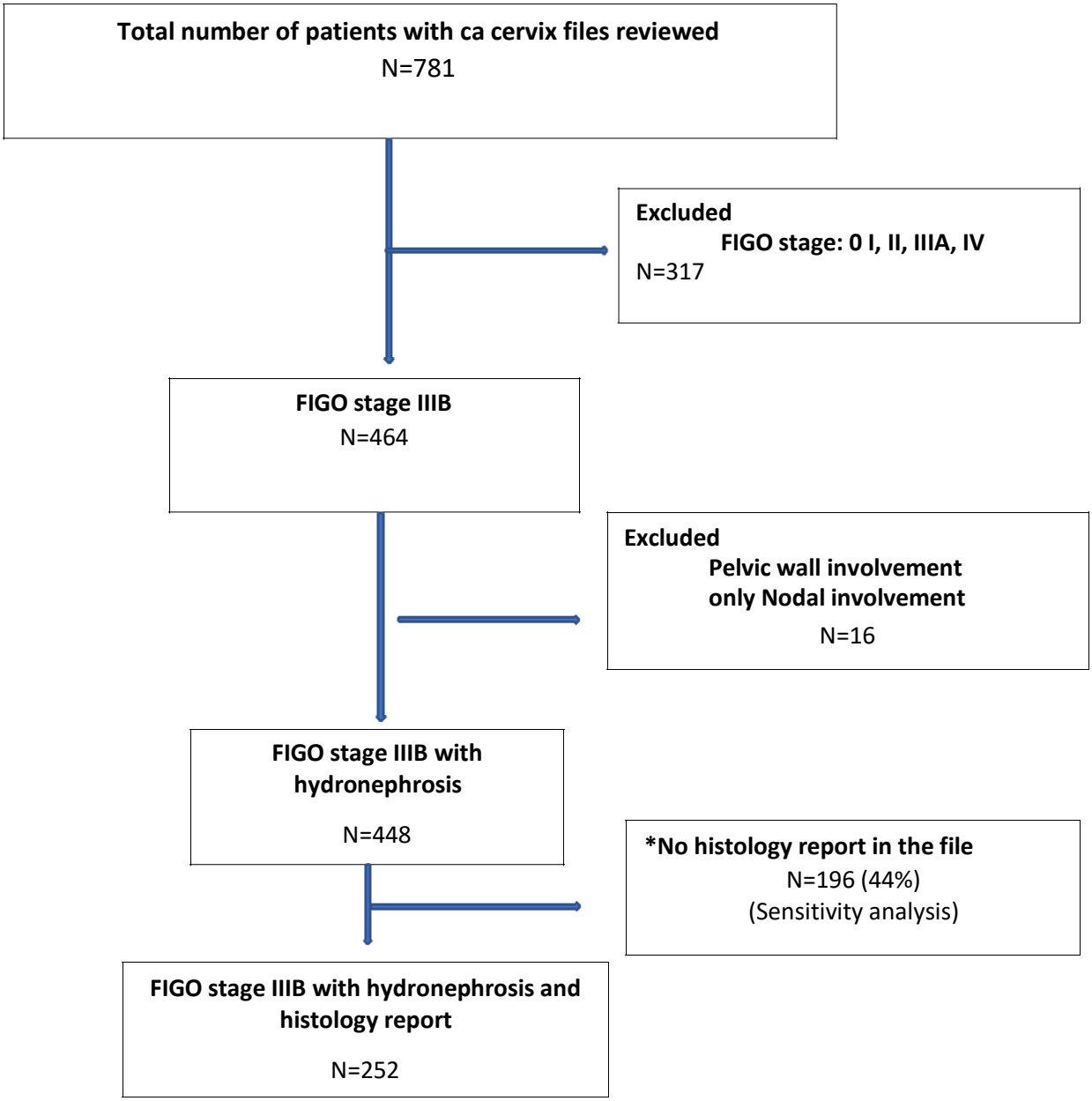
i. Missing data was a major study limitation, this was minimized by increasing the sample size, by 41%, available variables were analyzed, and a sensitivity analysis was carried on those who missed histology report in the files.
ii. Missing outcomes of patients who are lost to follow. Phone calls were made to patients to get outcome data. Those patients whose outcome data was still missing were censored in the analysis.

DISSEMINATION OF RESULTS

Results from this study were presented to the Department of Obstetrics and Gynecology at the University of Nairobi and Kenyatta National Hospital. Results from this study will also be published in a peer reviewed journal and presented in conferences and workshops.

CHAPTER 3: RESULTS

A total of 781 files were reviewed, out of which 464 files were inpatients with FIGO stage IIIB cervical cancer, after excluding those with pelvic wall involvement only and nodal involvement 448 patients were eligible for analysis for this study. A total of 196 (44%) files did not have histology reports in the patient files, they were used for sensitivity analysis. In all these cases where the histology report was not available in the file had cervical cancer, however there was a lack of consistency on how the histology report was worded in the file notes (**figure 1**).



*Those patients who had their histology written somewhere in the file notes, but without the actual histology report. In all cases, they had cervical cancer, but there was lack of consistency in the notes on how the histology report was worded

Figure 1: Eligibility schema of patients with cervical cancer stage IIIB with hydronephrosis admitted at Kenyatta National Hospital (KNH), 2012 -2017

The overall mean (SD) age for FIGO stage IIIB cervical cancer patients was 49.1(11.8) years. Most patients were married, Christian, with no formal employment, are of primary school level education wise and were registered for national health insurance fund (NHIF). Of note is the high percentage (up to 29%) of variables that were not documented (**table 1**)**.**

Table 1: Socio-demographic characteristics of patients with cervical cancer stage IIIB with hydronephrosis at Kenyatta National Hospital (KNH), 2012-2017

Variable	**N=448** **n(%)**
Age	
Mean (SD)	49.1 (11.8)
Marital status	
Single	102(23)
Married	**273(61**)
Separated	18(4)
Widowed	51(11)
Other	1(0.2)
Not documented	3(1)
Religion	
Muslim	6(1)
Christian	**434(97)**
Not documented	8(2)
Occupation	
None	**146(33)**
Casual Laborer	48(11)
Self-employed	114(25)
Formal Employment	18(4)
Not documented	**122(27)**
Education level	
No formal education	23(5)
Primary Level	**180(40)**
Secondary level	90(20)
College/University	27(6)
Not documented	**128(29)**
NHIF registered	
Yes	**264(59)**
No	176(39)
Not documented	8(2)

NHIF=National Health Insurance fund

Most patients ever used copper T intrauterine device and progesterone implants for family planning. Most patients are not smokers, are HIV negative and have no comorbidities. Of note is the high percentage (up to 30%) of variables that were not documented (**table 2**)**.**

Table 2: Clinical characteristics of patients with cervical cancer stage IIIB with hydronephrosis admitted at Kenyatta National Hospital (KNH), 2012-2017

Variable	**N=448** **n(%)**
Parity	
Median (IQR)	4 (3 -6)
***Ever used family planning method**	
Ever used IUCD- copper T	**59(13)**
Ever used IUCD- Mirena	6(1)
Ever used Depo Provera)	1(0.2)
Ever used progesterone Implant	**54(12)**
Ever used progesterone pills	16(4)
Ever used COC pill	0(0)
Ever used condoms	2(0.4)
Ever used natural methods	0(0)
Ever used family planning other	1(0.2)
	11(3)
Smoking	
Yes	10(2)
No	**306(68)**
Not documented	**132(30)**
HIV status	
HIV positive	95(21)
HIV negative	236(53)
Not documented	**117(26)**
Other comorbidities	
None	**275(61)**
Diabetes	3(1)
Hypertension	71(16)
Deep venous thrombosis	43(10)
Anemia	31(7)
Other	25(6)

*one patient can have ever used more than one method of family planning
IUCD=Intrauterine contraceptive device COC=combined oral contraceptive
HIV=Human immunodeficiency virus

A total of 252 patients had their histology report in the file. Out of these, 89% were squamous cell carcinoma. A high proportion (196/448) had no histology report in their files, the histology was written in the file notes with no consistency on how the cervical cancer histology was written in the notes. The reason given by the Records Department for the missing histology reports was the different filing systems by the Radiotherapy Department and the Gynecology Oncology Unit. The median (IQR) survival in months was 1.4(0.4-5.4). Most patients (55%) had their cancer treatment written as radiotherapy given, without specifying the dose, if it was external beam and or brachytherapy, and if concurrent chemotherapy was given. In addition, a number (34%) of them did not have the type of cancer treatment indicated in their files. With 89% (402/448) of the total sample not having their cancer treatment clearly indicated, it is difficult to clearly establish the radiotherapy treatment given (**table 3**).

Table 3: Histologic types and cancer treatment of patients with cervical cancer stage IIIB with hydronephrosis, admitted at Kenyatta National Hospital (KNH), 2012-2017	
Variable	**N=448 n(%)**
Histological type	
Squamous cell carcinoma	**224(50)**
Anaplastic carcinoma	2(0.4)
Adenocarcinoma	20(5)
***No histology report in the file**	**196(44**)
Other	6(1)
Histological type (N=252)	
Squamous cell carcinoma	**224(89)**
Anaplastic carcinoma	2(1)
Adenocarcinoma	20(8)
Other	6(2)
Median (IQR)	
Survival(months)	1.4(0.4-5.4)
#Cancer treatment offered	
External beam radiotherapy	9(2)
Brachytherapy	**51(11)**
Chemoradiation	92(21)
Radiotherapy given not specified	**248(55)**
Cancer treatment given not indicated	154(34)
* These are patients who had their histology written somewhere in the file notes, but without the actual histology report. In all the cases, they had cervical cancer, but there was lack of consistency in the notes on how the histology report was worded # It was difficult to collect data on cancer treatment offered. This is because the patients have different files and filling systems for the Gynecology Oncology Unit and the Radiotherapy Department. One patient can receive more than one treatment	

Hydronephrosis in cervical cancer FIGO stage IIIB patients in Kenyatta National Hospital is mainly (79%) diagnosed by ultrasound. Of note, is several patients whose mode of diagnosis is not documented or not clear (53/448). Most (75%) patients present with bilateral hydronephrosis. Over 80% (361/448) have their hydronephrosis not graded. Over 60% (272/448) of patients did not have any decompression for their hydronephrosis. When relieve of hydronephrosis was offered 28% and 11% received nephrostomy tube and double J stent respectively. Dialysis was only offered to 17% of patients (**table 4**).

Table 4: Management of hydronephrosis in patients with cervical cancer stage IIIB with hydronephrosis, admitted at Kenyatta National Hospital (KNH), 2012-2017	
Variable	**N=448 n(%)**
Mode of diagnosis of hydronephrosis	
Ultrasound	**354(79)**
CT scan	25(6)
MRI	9(2)
Other	60(13)
Other modes of diagnosis of hydronephrosis (N=60)	
Clinical diagnosis	
Not documented	3(5)
Not clear	**44(73)**
Renal Review	9(15)
	4(7)
Symmetry status of hydronephrosis	
Unilateral	85(19)
Bilateral	**338(75)**
Not documented	25(6)
Hydronephrosis grade	
Mild (grade 1 and 2)	32(7)
Moderate (grade 3)	39(8)
Severe (grade 4)	16(4)
Not graded	**361(81)**
Method of decompression of hydronephrosis	
Nephrostomy tube	
Double J stent	126(28)
No decompression	49(11)
	272(61)
Dialysis	
Yes	77(17)
Not applicable	**238(53)**
No documented	133(30)

Patients who received decompression for hydronephrosis have better two and five-year survival compared to those who did not, though only by a few days, log rank test p= <0.001(**figure 2**). Patients with their histology report in the file have better two and five-year survival compared to those without their histology report in the file, log rank test p= <0.001 (**figure 3**).

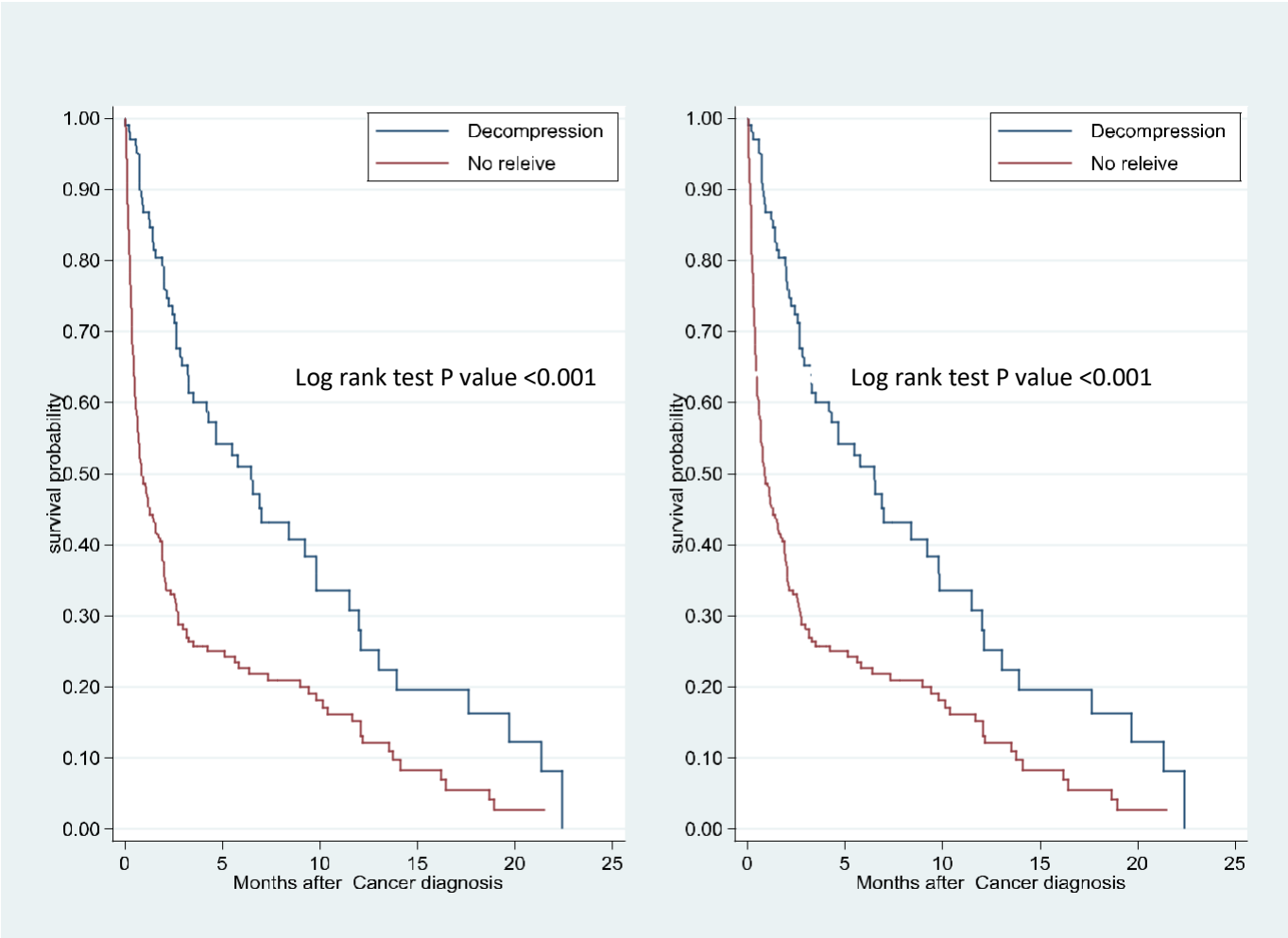


Figure 2: Two- and five-year survival for patients with cervical cancer stage IIIB and hydronephrosis, who had decompression for hydronephrosis versus those who did not have, admitted at Kenyatta National Hospital (KNH), 2012-2017

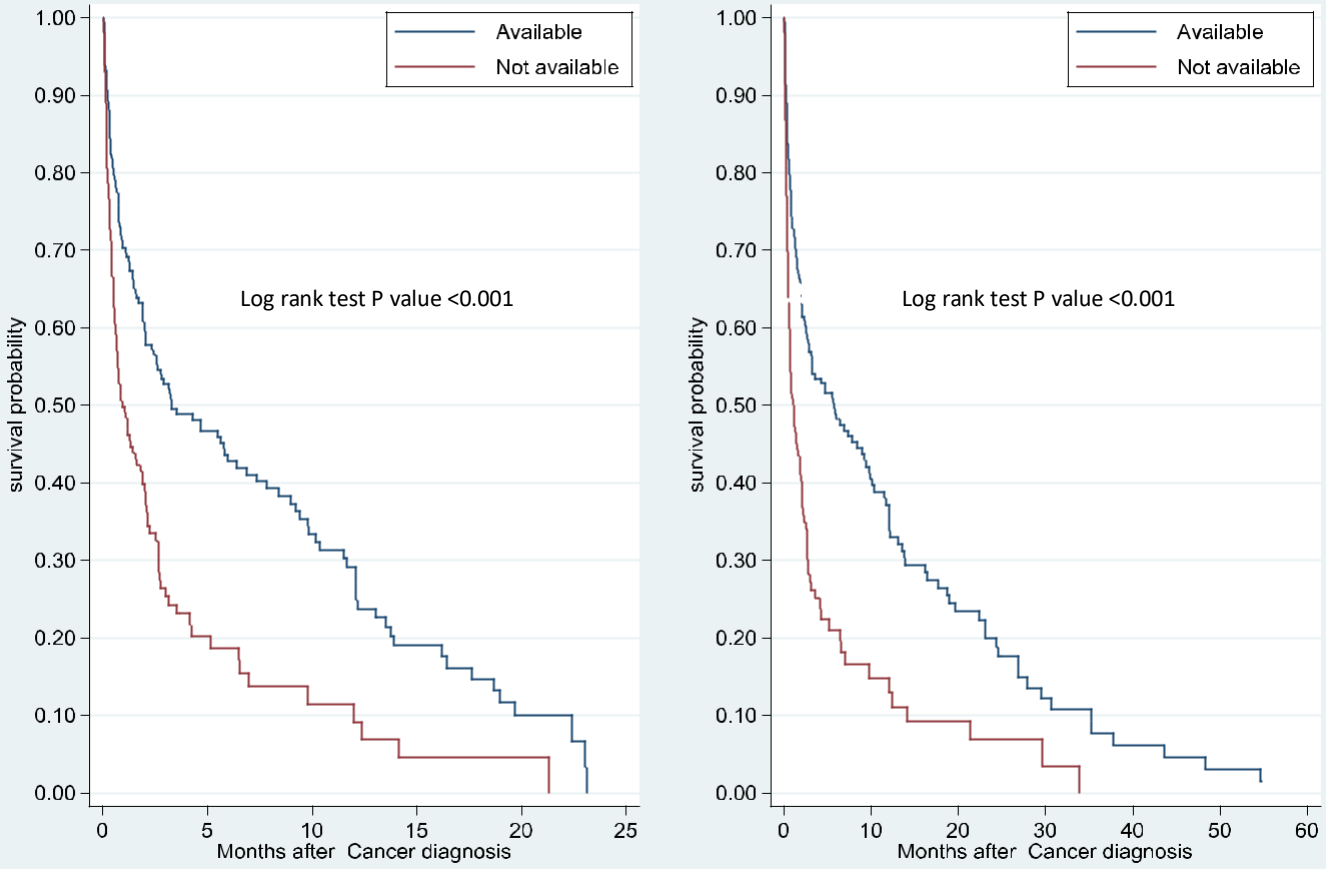


Figure 3: Two- and five-year survival for patients with cervical cancer stage IIIB and hydronephrosis, who had their histology report in the file versus those who did not have their histology report in the files, admitted at Kenyatta National Hospital (KNH), 2012-2017

CHAPTER 4: DISCUSSION

This study evaluated the management and survival of inpatient FIGO stage IIIB cervical cancer patients admitted and managed at KNH between 2012 and 2017, with two sub-analyses of comparing a) 2 and 5-year survival of those who received hydronephrosis decompression versus no compression and, b) 2 and 5-year survival of those who had the histology report in the file versus those who did not have.

Squamous cell carcinoma, was the commonest histological type among those who had histology reports in the files. Our finding is like the 2008-2010 cohort in this same setting (3). A high proportion of patients had written histology in their files, without the histology report.

Most patients received radiotherapy treatment, though the specifications of the radiotherapy treatment given in terms of dose and cycles was not clear. This finding can be explained in part, by the fact that the Departments of Radiotherapy and Obstetrics and Gynecology run two different records systems that are not linked. Concurrent chemoradiotherapy is the standard treatment for FIGO stage IIIB cervical cancer (32-37). From our findings it was difficult to get the details of how radiotherapy was given. Lack of linkage between the records of the two Departments may negatively impact on patient outcomes.

Hydronephrosis was commonly diagnosed by ultrasound, bilateral, not graded, and not decompressed. When decompression was offered, nephrostomy tube was the commonest method. Only few patients received dialysis. Worsening morbidity in patients with cervical cancer FIGO stage IIIB is due to acute renal injury, especially in

those with bilateral hydronephrosis (4, 5, 7, 8). Patients with bilateral hydronephrosis require immediate decompression, to avoid renal complications including uremia (21-23). It is surprising, that most of the patients in our cohort did not receive any decompression of their hydronephrosis, yet most were bilateral.

The overall median survival in months (IQR) is 1.4(0.4-5.4). Those who received decompression for hydronephrosis had better 2 and 5-year survival compared to those who did not, though by a few days. Patients who had their histology report in the files had better 2 and 5-year survival compared to those who did not have their histology report in the file. The median survival is way worse than the 15 months found in 2008-2010 KNH study(3). The reasons for the worse survival were outside the scope of this study and were not explored. We suggest that the patients in the 2008-2010 study were ambulatory and receiving radiotherapy unlike our cohort, where the patients are admitted waiting for decompression before radiotherapy or have had to discontinue radiotherapy.

The reasons for better 2 and 5-year survival in patients who had their histology report in the files compared to those who did not have their histology report in the file, are not clear. We postulate that delays in treatment could have occurred in patients without the histology report. There is a likelihood that these patients had to be rebooked as they went to find the histology report. It could also have been an incidental finding.

None documentation was as high as 30% in some variables. This is similar, to the 1998-2008 cohort of cancer of the ovary patients in this same setting (38). Poor

documentation poses challenges in patient management. The oncology unit is paper based and lacks standardized encounter forms.

The main limitation of this study is a high percentage of missing data and the lack of linkage between the records in the Gynecologic Oncology Unit and the Radiotherapy Unit. Despite this limitation, this is the first study in Kenya and the region describing management and outcomes in FIGO stage IIIB cervical cancer patients. The calculated sample size was also achieved.

CONCLUSION

Squamous cell carcinoma is the commonest histologic type in inpatient FIGO stage IIIB cervical cancer patients with hydronephrosis admitted and managed at KNH between 2012 and 2017. Radiotherapy treatment was not clearly indicated in most, had bilateral hydronephrosis and decompression was not offered for many patients. The overall median survival in months (IQR) was 1.4(0.4-5.4). Though patients who received decompression for hydronephrosis had better survival, this is only by a few days. Decompression of hydronephrosis should not delay definitive chemoradiation therapy.

RECOMMENDATIONS

1. Link the records departments of Gynecologic Oncology and the Radiotherapy units for better patient management and follow up
2. Electronically link the pathology Department with the Gynecologic Oncology Unit to allow access to the pathology reports

3. Structure and standardize encounter forms to improve on reporting and documentation. Invest on an electronic capture of patient encounters. This will allow checks and balances to reduce on missing information.
4. Offer decompression to all patients with bilateral hydronephrosis where possible to reduce on renal complications but should not delay the definitive chemoradiation therapy.

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CHAPTER 6: APPENDIXES

APPENDIX 1: DATA ABSTRACTION FORM

DATA ABSTRACTION FORM

MANAGEMENT AND SURVIVAL OF STAGE IIIB CERVICAL CANCER WITH HYDRONEPHROSIS ADMITTED AT KENYATTA NATIONAL HOSPITAL, 2012-2017

SECTION A: IDENTIFIERS

Hospital IP No:	**Study Number:**

SECTION A: ELIGIBILITY TO STUDY

1) **File available in the Records Department** ( ) Yes*(move to 2)*
   ( ) No*(exclude from study)*

2) **Confirmed diagnosis of cervical cancer, histopathology report available** ( ) Yes*(move to number 3)*
   ( ) No*(exclude from the study)*

3) **The histopathology report is dated**
   ( ) Yes*(record date and move to 4)* __/__/__ (dd/mm/yy)
   ( ) No (exclude from study)

4) **Cervical cancer FIGO stage III on admission (exclude all stage I, II, and IV)** ( ) Yes*(move to number 5)*
   ( ) No (exclude from the study) Indicate stage……

5) **Does the patient have involvement of lower 1/3 Vagina and***(check radiological investigations to confirm)*
   ( ) Hydronephrosis alone*(move to section B)*
   ( ) Hydronephrosis and pelvic wall involvement *(move to section B)*
   ( ) Hydronephrosis and pelvic/paraaortic nodes *(exclude from study)*
   ( ) Pelvic wall involvement only*(exclude from the study)*
   ( ) Pelvic and paraaortic nodes only*(exclude from the study)*

( ) Not Indicated *(exclude from the study)*

Summary of eligibility criteria

All FIGO stages of cervical cancer admitted in KNH, 2012-2017

Exclude:
- Missing file
- No histopathology report
- Histopathology report not dated
- FIGO stages I, II and IV
- FIGO stage IIIB with pelvic wall extension only
- FIGO stage III with pelvic and paraaortic nodes

Study sample
FIGO stage IIIB with hydronephrosis

SECTION B: SOCIO-DEMOGRAPHIC DATA

1) **Date of birth: DD/MM/YY**
__/__/__ ( ) Not indicated

2) **Age in years** _____ **( )** Not indicated

3) **Marital status**
( ) Single
( ) Married
( ) Separated
( ) Widowed
( ) Other*(specify)* ----------
( ) Not indicated

4) **Religion**
( ) Muslim
( ) Christian
( ) Other*(specify)* ----------
( ) Not indicated

5) **Occupation**
( ) None
( ) Casual Laborer
( ) Self-employed
( ) Formal Employment
( ) Not indicated

6) **Education level**
( ) No formal education
( ) Primary Level
( ) Secondary level
( ) College/University
( ) Not indicated

7) **NHIF registered**
( ) Yes ( )
No
( ) Not indicated

SECTION C: CLINICAL CHARACTERISTICS

Past Medical History

1) **Parity**
Para ____ + _____ ( ) Not indicated

2) **Family planning**
( ) None
( ) IUCD- copper T
( ) IUCD- Mirena

( ) Depo provera
( ) Implant
( ) Progesterone pills
( ) Combined oral contraceptive pill
( ) Condoms
( ) Natural methods
( ) Other *(Specify)*…….
( ) Not indicated

3) Smoking

( ) Yes
( ) No
( ) Not indicated

4) HIV status

( ) HIV positive
If positive:
Lowest recorded CD4 counts ……. ( ) Not indicated
Highest recorded viral load …… ( ) Not indicated
( ) HIV negative
( ) HIV status not indicated

5) Other comorbidities

( ) None
( ) Diabetes
( ) Hypertension
( ) Deep venous thrombosis
( ) Anemia
( ) Other*(Specify)*…….

Time to events

1) Date of cancer diagnosis (date recorded in histopathology report)

( ) Yes (record date and move to 2) __/__/__ (dd/mm/yy)
( ) Not indicated (go back to section A (3) and exclude the file)

2) Date of first clinic/hospital visit

( ) Yes (record the date) __/__/__ (dd/mm/yy)
( ) Not Indicated

3) Date of FIGO stage III diagnosis

__/__/__ (dd/mm/yy)

4) Date of first FIGO staging (if it was less than stage IIIB at some point) __/__/__ (dd/mm/yy) (specify)…..

5) Date of FIGO staging (if was later staged more than IIIB)

__/__/__ (dd/mm/yy) (specify)…..

6) Patient alive or dead

( ) Alive

Date of last follow up clinic __/__/__ (dd/mm/yy)

( ) Dead

Date of death __/__/__ (dd/mm/yy)

Date of last follow up clinic __/__/__ (dd/mm/yy)

( ) Not clear*(indicate why)*……..

7) Date of diagnosis of hydronephrosis

__/__/__ (dd/mm/yy)

( ) Not indicated

8) Date of Insertion of nephrostomy tube __/__/__ (dd/mm/yy)

( ) Not applicable

( ) Not indicated

9) Date of insertion of DJ stent

__/__/__ (dd/mm/yy)

( ) Not applicable

( ) Not indicated

10) Date of Dialysis

__/__/__ (dd/mm/yy)

( ) Not applicable

( ) Not indicated

FIGO Staging

1) Confirm this is FIGO stage III B with Hydronephrosis

( ) Yes, it is FIGO stage IIIB with hydronephrosis

( ) No, it is not FIGO stage IIIB with hydronephrosis*(go back to section A5, and exclude from study)*

2) How was FIGO staging done*(Tick all that apply)*

( ) Examination Under Anesthesia

( ) Done in KNH

( ) Done outside KNH

( ) Not Indicated

( ) Examination without Anesthesia

( )Done in KNH

( )Done outside KNH

( )Not indicated

( ) MRI

( ) Ultrasound

( ) Not Indicated, referred with staging

( ) Other (*specify)* …..

3) **FIGO stage progressed from the admission FIGO stage**

( ) Not progressed

( ) Progressed

If progressed

Indicate progressed stage ……

Indicate date of progressed stage __/__/__ (dd/mm/yy) How was diagnosis of progression made*(specify)*……

Histopathology

1) **Histological type (check on histopathology report)**

( ) Squamous cell carcinoma (SCC)

If SCC tick all that apply

( ) Well differentiated

( ) Moderate differentiated

( ) Poorly differentiated

( ) Keratinizing

( ) Non-keratinizing

( ) Large cell

( ) Small cell

( ) Other*(specify)*…..

( ) Anaplastic Carcinoma

( ) Adenocarcinoma

( ) Sarcoma of Cervix

( ) Other*(specify)*…….

SECTION D: MANAGEMENT OF HYDRONEPHROSIS

1) **Date of diagnosis of hydronephrosis**

__/__/__ (dd/mm/yy)

2) **Mode of diagnosis of hydronephrosis (Tick all that apply)**( ) Ultrasound

( ) CT scan

( )MRI

( ) Other*(specify)* …….

3) **Symmetry status of hydronephrosis**

( ) Unilateral

( ) Bilateral

4) **Hydronephrosis grade**

( ) Normal (grade 0)

( ) Mild (grade 1 and 2)

( ) Moderate (grade 3)

( ) Severe (grade 4)

( ) Not graded

5) **Renal injury, what is the highest recorded before treatment** ( ) Urea

( ) Creatinine (

) Potassium

6) Renal functions after treatment, what is the lowest recorded

( ) Urea
( ) Creatinine
( ) Potassium
( ) Not recorded

7) Relieve of hydronephrosis*(Tick all that apply)*

( ) Nephrostomy tube
( ) DJ stent
( ) No relieve

8) Dialysis

( )Yes
( ) No

SECTION E: CANCER TREATMENT

1) Cancer treatment offered (Tick all that apply)

( ) External beam radiotherapy (EBRT)
( ) External boost
( ) Brachytherapy
( ) Chemotherapy (cisplatin)
( ) Chemotherapy other*(specify)* ….
( ) Written radiotherapy given no specifications
( ) Not indicated

SECTION F: PHONE CALL DATA

1. **Date of last clinic /hospital visit**

__/__/__ (dd/mm/yy)

2. **Date of death**

__/__/__ (dd/mm/yy)

APPENDIX 2: TIMELINES AND BUDGET

TIMELINES

Timelines											
#	Activity	2020						2021			
		Jul	Aug	Sept	Oct	Nov	Dec	Jan	Feb	Mar	April
1.	Proposal Development										
2.	Development of Redcap software										
3.	Ethics review and approval										
4.	Prepare for data collection-training and tool testing										
5.	Data collection										
6.	Data analysis										
7.	Project write up										
8.	Presentation to Department and dissemination of results										

BUDGET

Components	Unit of Measure	Duration/ Number	Unit Cost (Kshs)	Total Cost (Kshs)
Personnel				
Research Assistant	2	2.5	50,000	**250,000.00**
Statistician	1	1	60,000	**60,000.00**
Sub-total				**310,000.00**
Printing				
Questionnaires	1	6	10	**60.00**
Final Report	1	100	10	**1000.00**
Sub-total				**1,060.00**
Photocopying				
Questionnaires	10	6	2	**120.00**
Final Report	10	100	2	**2000.00**
Final Report Binding	1	10	200	**2000.00**
Sub-total				**4,120.00**
Other costs				
ERC Fees	1	1	2,000	2,000.00
REDCap Database design and hosting	1	1	20,000	20,000.00
Phone calls	414	1	50	20,700.00
Records Access Fee	1	1	1,500	1,500.00
Poster Printing	1	1	2,500.00	2,500.00
Sub-total				**26,000.00**
Total				**361, 880.00**

APPENDIX 3: VERBAL CONSENT

PHONE CALL VERBAL CONSENT-ENGLISH
MANAGEMENT AND SURVIVAL OF STAGE IIIB CERVICAL CANCER WITH HYDRONEPHROSIS ADMITTED AT KENYATTA NATIONAL HOSPITAL, 2012-2017
I am Dr Rose Kosgei, the lead researcher in a study looking at management of cervical cancer patients, stage III B with urine obstruction at Kenyatta National hospital. This study will evaluate 414 patients who have been in care since 2012, and you are one of them. Your phone number is listed in the file. I am calling because I need your assistance to clarify some of the information that is missing or unclear from your file. This information will help us complete the study and understand how to manage patients with cervical cancer stage IIIB with urine obstruction better. This study has been approved by Kenyatta National Hospital/University of Nairobi Research and Ethics Committee. The ethics committee has granted access to your file. None of your identifying information will be collected. Information collected will be used only for purposes of this study. Your information will be kept confidential. Please note that the call may be recorded for reference purposes. The phone call will last a maximum of five minutes. Should you choose not to give any information or stop giving information at any point, it will not affect care given to you or your loved one at Kenyatta National Hospital. Do you have any questions/clarifications? I would be happy to answer the questions or clarify any concerns.

Would you be willing to participate in the study and answer some questions on phone? ( ) Yes ( ) No

IDHINI YA MATAMSHI YA SIMU

USIMAMIZI NA UPONAJI WA SARATANI YA KIZAZI DARAJA LA IIIB NA HYDRONEPHROSIS KWA WALOLAZWA HOSPITALI YA KITAIFA YA KENYATTA KIPINDI CHA 2012-2017

Mimi ni Dkt. Rose Kosgei, mtafiti mkuu anayeongoza uchunguzi unaoangazia usimamizi wa wagonjwa wa saratani ya kizazi waliofikia hatua ya IIIB na kizuizi cha mkojo katika hospitali ya kitaifa ya Kenyatta. Utafiti huu utawatathmini wagonjwa 414 waliokua chini ya uangalizi tangu mwaka 2012, na wewe ni mmoja wao. Namba yako ya simu imeorodheshwa katika faili. Nakupigia simu kwa sababu nahitaji msaada wako wa ufafanuzi zaidi wa habari ambayo haipo au haifahamiki wazi kutoka kwenye faili yako. Taarifa hio itatusaidia kuumaliza utafiti na kuelewa namna ya kuwasimamia wagonjwa walio na saratani ya kizazi hatua ya IIIB na uzuiaji wa mkojo, vyema. Utafti huu umeitishwa na kamati ya kitaifa ya hospitali ya kitaifa ya Kenyatta/kituo cha utafiti na maadili cha Chuo kikuu cha Nairobi. Kamati ya maadili imepeana ruhusa kutumiwa faili yako. Hakuna taarifa ya utambulisho wako itakayokusanywa. Habari iliyokusanywa itatumika tu kwa madhumuni ya utafiti huu. Taarifa zako zitawekwa siri. Tafadhali fahamu kuwa mazungumzo ya simu yanaweza kurekodiwa kwa sababu ya kumbukumbu. Mazungumzo hayo ya simu yatadumu kwa dakika tano. Iwapo utachagua kutotoa habari yeyote au kuacha kutoa habari wakati wowote, hakutoathiri huduma uliyopewa au kwa jamaa yako mpendwa katika hospitali ya kitaifa ya Kenyatta. Je, una swali lolote au ufafanuzi? Nitafurahi kuyajibu maswali yako au kufafanua wasiwasi wowote. Je, ungependa kushiriki katika utafiti na kujibu maswali kadhaa kupitia simu? ( ) Ndio ( ) La

APPENDIX 4: ETHICS APPROVAL

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES

KNH-UON ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202

Ref: KNH-ERC/A/392

12th November 2020

Dr. Rose Jepchumba Kosgei
Reg. No.H117/27758/2019
(Fellowship in Gynecologic Oncology)
Dept.of Obstetrics and Gynaecology
School of Medicine
College of Health Sciences
University of Nairobi

KENYATTA NATIONAL HOSPITAL
APPROVED
12 NOV 2020
KNH/UoN-ERC

Dear Dr. Kosgei

RESEARCH PROPOSAL – MANAGEMENT AND SURVIVAL OF STAGE IIIB CERVICAL CANCER WITH HYDRONEPHROSIS ADMITTED AT KENYATTA NATIONAL HOSPITAL, 2012-2017 (P487/09/2020)

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 12th November 2020 – 11th November 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.

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