THE UNIVERSITY OF ZAMBIA
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DEPARTMENT OF OBSTETRICS & GYNAECOLOGY

A COMPARATIVE STUDY ON BEDSIDE AND EXAMINATION UNDER ANEASTHESIA CLINCAL STAGING METHODS FOR CERVICAL CANCER AT UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA

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DECLARATION

I **Abby Makukula,** hereby declare that the dissertation represents my own work, and that it has not previously been submitted for a degree, diploma or other qualification at this or any other University

Signature…… **Date**……

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Dr. M. Mwanahamuntu

CERTIFICATE OF APPROVAL

This dissertation of **ABBY MAKUKULA** has been approved as partial fulfillment of the requirements for the award of Master of Medicine in Obstetrics and Gynaecology by the University of Zambia

INTERNAL EXAMINER I

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Signature **Date**

INTERNAL EXAMINER II

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EXTERNAL EXAMINER

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ABSTRACT

Cervical cancer universally is clinically staged using the FIGO staging system performed on examination under anaesthesia (EUA). The EUA staging method is no longer thought to be mandatory but optional in staging cervical cancer. This is emerging from the on-going debate within scientific communities involved in cervical cancer management who are challenging the EUA method for bedside method. The on-going debate indicates that bedside method to stage cervical cancer be employed. However, there is still a grey area on published literature that is known on the method in terms of patient selection criteria, the sensitivity, positive predictive value and its accuracy. This may be limiting its use by clinicians who may want to employ the method. This study's objective was to compare the bedside staging method to the current standard staging method (EUA) for cervical cancer.

After ethical approval, a prospective cross section study was conducted at University Teaching Hospital (UTH), Lusaka from December 2013 to April 2014 on suspected cervical cancer patients. Twenty-three participants were recruited and data was collected using a paired data test technique. The suspected cervical cancer patients were subjected to two independent staging method- first a bedside staging and then an EUA by a clinician at the level of Registrar and above who was not aware of the findings of the bedside staging. Data was collected using a coded checklist linking data from same patient. Analysis was done using SPSS 17 statistical package. The sensitivity test, positive predictive value and the accuracy of the bedside method was calculated. Further analysis for correlation test was done.

The age range of the participants was from 34 to 79 with a mean age of 51.5 years. The calculated sensitivity and positive predict value of the method was 87.5%, and 67% respectively with an accuracy of 64%. The findings are based on a small sample size recruited from one large clinical site and hence could not be generalized. However, the findings have presented an opportunity for further research on the subject. The staging of cervical cancer using EUA should not be abandoned until sufficient evidence on the accuracy and safety of the alternate bedside method is collected. For patients who are not suitable for anaesthesia and cannot undergo EUA, the bedside method is an optional method but administration of analgesia and /or anxiolytic before the staging procedure is advisable to reduce the patient related factors like pain and poor cooperation that may affect the staging process. For patients assigned to lower stages (2 or lower) on bedside method, further EUA staging is recommended because of either under or over staging on the bedside method.

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"*Only a life lived for others is a life worthwhile"*
(Albert Einstein 1879-1955)

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LIST OF ABBREVIATIONS

AIDC	Adult Infectious Disease Control
CaCx	Cancer of the Cervix
CD	Cluster Differentiation
CDH	Cancer Disease Hospital
CI	Confidence Interval
CT	Computerized Tomography
CXR	Chest X-ray
EUA	Examination under Anaesthesia
FIGO	International Federations of Gynecology and Obstetrics
FN	False Negative
FP	False Positive
FPR	False Positive Rate
HAART	Highly Active Anti retroviral Treatment
HIV	Human Immuno-deficiency Virus
HPV	Human Papillomavirus
ICC	Invasive Carcinoma of the Cervix
IVP	Intravenous Pyelography
MRI	Magnetic Resonance Imaging
N	Number
PPV	Positive Predictive Value
GPPF	Graduate Proposal Presentation Forum
TN	True Negative
TP	True Positive
TPR	True Positive Rate
UICC	International Union against Cancer
US	Ultrasonography
UTH	University Teaching Hospital
WHO	World Health Organization

Dedication

To my late father who always emphasized on excellence in everything at all times

CHAPTER ONE

1.1 INTRODUCTION

The clinical staging system for cervical cancer currently employed by International Federation of Gynaecology and Obstetrics (FIGO) has attracted a lot of debate among cervical cancer specialist and the scientific community regarding different aspects of cervical cancer staging, namely clinical versus surgical staging, or bedside staging versus examination under anaesthesia (EUA) (Mutch, 2009*)*. Critics have argued that the current staging system by examination under anaesthesia is not mandatory to cervical cancer staging but optional.

Cancer staging is a clinical assessment to determine the extent of cancer growth and spread from the primary site of the disease to the surrounding structures and/or distant organ metastases. The purpose of staging a cancer is to offer a classification of the extent of cancer to provide a method of conveying clinical experience to others for comparison of treatment methods without confusion or ambiguity and not a mechanism to assign treatment (Pecorelli et al, 2003; Moore, 2006; Eifel et al, 2009*).* Currently, the FIGO staging system for cervical cancer performed on examination under anaesthesia (EUA) is the widely used staging classification for cervical cancer, and it is based on clinical evaluation of the tumour size and extent of disease spread from the cervix (the primary site) to surrounding structures in the pelvis (Moore, 2006; Creasman, 1995*).*

The FIGO clinical staging system for cervical cancer was developed by International Federation of Gynaecology and Obstetrics (FIGO) in corroboration with World Health Organization (WHO) and the International Union against Cancer (UICC)**.** The FIGO staging system recommended that cervical cancer should continue being staged clinically and not surgically to allow evaluation of the cancer for treatment comparison in developing countries where the cancer disease is commonest.

The current FIGO clinical staging system for cervical cancer is based on a speculum visualisation and bimanual palpation examinations of the vagina, cervix and pelvis together with a rectal examination for cancer spread performed on examination under anaesthesia. The centres with available resources have an option of employing additional examinations like colposcopy, cystoscopy, endocervical curettage, hysteroscopy, ultra-sound, Chest X-ray, CT and MRI. However, in many low resource settings, speculum and

bimanual palpation examinations of the vaginal/pelvis, and rectal examination are the only feasible approach to staging during examination under anaesthesia (Sellor and Sankaranarayanan, 2000). Cystoscopy, sigmoidoscopy and intravenous pyelogram (IVP) previously employed are no longer regarded mandatory investigations to cervical cancer staging but optional according to revised FIGO staging of cervical cancer (Mutch, 2009; Pecorelli et al. 2009; Jeong et al 2012).

The FIGO clinical staging method for cervical cancer classification is from I to IV. In stage I disease, the cancer lesion is confined to the cervix; stage II involves cancer spread beyond the cervix to the upper vagina and /or parametrial tissues; stage III involves further cancer spread to the lower vagina or/and pelvic wall; and stage IV is cancer spread to pelvic structures and beyond true pelvis (Pecorelli et al. 2000). The stages have sub-stages of the disease. Stage I is divided into IA and IB, where IA is diagnosed histopathologically on biopsy while stages IB to V are macroscopic with visible cancer lesions and allows for clinical staging.

The FIGO staging recommends that cancer staging system should be evidence based and user friendly. The staging should be based on the best available knowledge at hand and changes should only occur over time based upon development or acquisition of further new knowledge**.** However, high levels of evidence are not always available for certain situations (Percorelli et al., 2000*)*. The FIGO committee on gynaecologic oncology in "Principles of Cancer Staging" describes a good staging system as one with *validity, reliability* and *practical* basic characteristics. *Validity* described as "staging system that allows for the creation of groups of cases that experience similar outcomes while at the same time reflecting a full range of possible presentations for that particular type of cancer". The system must be flexible to adapt to important changes in medical care. *Reliability* described as "staging system that ensures that identical cases are always assigned the same staging category, and without ambiguity but based on as far as possible measurable entities that are objectively evaluated". *Practical* described as "systems suitability for day to day use in a wide range of clinical environments and not requiring diagnostic procedures that are not readily available to most practitioners, or extraordinary expertise or knowledge with regard to a particular malignancy" (Pecorelli et al, 2000; Pecorelli et al, 2003).

This study aimed to compare bedside staging with examination under anaesthesia (EUA) staging (considered the gold standard for cervical cancer staging), as regards to accuracy and patient feedback.

1.1.2 Background information

Scope of cervical cancer problem globally, regionally and locally

Cervical cancer is the commonest gynaecological cancers in women that results from long-term persistent infection of Human Papillomavirus (HPV) (Hacker et al., 2010*;* Schorge et al, 2008). Multiparous women are affected more (Franco et al, 2003) because of the increased risk of exposure to HPV. The World Health Organization (WHO) has ranked cervical cancer as the leading cause of death among women, and the gravest threat to women's lives in the world. After breast cancer, it is the second commonest cause of cancer among women (Franco et al. 2003). Annually, there are over 500,000 new cases of cervical cancer resulting in 260,000 deaths worldwide and an estimated one million (or more) cases worldwide are undiagnosed (WHO, 2006). Over 90 percent of most of these cases occur in developing countries where resources to prevent, stage and treat the disease are scarce (WHO, 2006).

Sub-saharan Africa, where Zambia is located, has the highest cervical cancer disease burden and the world highest age standardized cervical cancer death rates. According to WHO/ICO, Zambia has 1839 diagnosed cervical cancer cases annually and 1276 die from the disease. It is the commonest female malignancy cancer in Zambia with an annual crude incidence rate of 29.1 per 100,000 female of all ages. Other studies have cited Zambia to have one of the highest age-standardized incidence rates of cervical cancer in Africa, estimated at 54 cases per 100,000 women per year, and the associated mortality rate of 44 deaths per 100,000 women per year. The majority of cases are diagnosed in the 15 to 44 years age group (Liu et al. 2012; WHO/ICO, 2010).

1.2 STATEMENT OF THE PROBLEM

Cervical cancer is the commonest female malignancy and a leading cause of death in Zambia and the developing world. There are over one million estimated cases worldwide and most are undiagnosed (WHO, 2006). The review of UTH theatre records for the three year period 2009 to 2011, showed a total of 1594 cervical cancer cases were clinical staged on examination under anaesthesia (EUA) accounting for 30 to 40 percent cases on gynaecology theatre lists. Staging cervical cancer on examination under anaesthesia requires the cases to compete for theatre space and time already strained with other gynaecological surgical cases.

The examination under anaesthesia staging method for cervical cancer has other challenges in term of cost for theatre consumables, in patient care for bed space, nursing procedures and food during admission for pre anaesthetic evaluation and correction of anaesthetic risk where exists and possible. In addition there is the requirement of functional theatre facilities and space and theatre support staff for procedure to be preformed. This in many limited resource setting where the burden of cervical cancer is largest, is not always available and often may be at the expense of other patients in need of surgery as a primary treatment.

Commonly, patients with cervical cancer present with a complication like severe anaemia resulting from repeated continuous bleeding from the necrotic tumour (Movva et al., 2009) and in the absence of HIV often present in very elderly patients they may pose a risk to anaesthesia. The attempt to correct conditions like anaemia through blood transfusion to reduce risk to anaesthesia sometimes results in delays in initiating treatment. Blood may not be readily available and failure to correct the anaesthetic risk results in staging (by EUA) ending up as a barrier to treatment. The procedures that were considered mandatory like cystoscopy and sigmoidoscopy, which requires EUA to be performed, have been classified as optional to the clinical staging of cervical cancer.

However, the critics in favour of EUA staging method argue that examination under anaesthesia allow for pelvic muscle relaxations during speculum and bimanual pelvic examination. Critics have argued that the current FIGO clinical staging system employed performed on examination under anaesthesia is not mandatory to cervical cancer staging but optional (Mutch, 2009). Yet many centres especially in limited resources setting like the University Teaching Hospital (UTH) have continued staging all cervical cancer

patients using examination under anaesthesia staging method at the expense of other patients who might really need the resources associated with theatre use. These resources can be saved and channelled to the care of other patients.

1.3 STUDY JUSTIFICATION

There is evidence that many centres use the bedside staging method to stage cervical cancer. There is an ongoing debate and discussion by many clinicians in different fora and yet there are no studies so far in the literature review that have been published to compare the bedside staging method to EUA - the gold standard cervical cancer staging method. Studies on other staging methods like imaging have been done. Yet the bedside method remains a grey area. A lot on the bedside method is not known, e.g. the sensitivity, specificity, the positive predictive value, the accuracy. The patient selection criteria for the method, the limitations of the staging method are not defined.

This study aimed to generate baseline date for future research on the method and for developing protocols on the staging method for cervical cancer. If the study were to demonstrate similar staging results as the examination under anaesthesia staging method, it woud cut on time and process to stage the cervical cancer patients and initiate them of treatment. Many institutions especially in resource constraint will be able to save resources and time. Cervical cancer patients not suitable for EUA due to risk of anaesthesia will have an option to be staged using the bedside method. The bedside method compared to other staging methods like the imaging method and EUA is cheaper and very suitable to constrained resource setting. The bedside method is able to accomplish the clinical staging object for cervical cancer.

Using the bedside staging method as an option in cases where general anaesthesia is contraindicated to a patient or theatre facilities is compromised due to shortage of theatre staff and consumables, can lead to a reduction in delays and/or eliminate barriers to treatment. Increased morbidity and early mortality will be reduced leading to future benefits to cervical cancer patients.

The aim of the study is to generate knowledge on bedside staging method, bridge up the knowledge gap, identify the clinical limitation(s) and use data to develop a guideline protocol on the use of the staging method for cervical cancer.

1.4 RESEARCH QUESTION

Is there a difference in the cervical cancer stage results obtained from the use of bedside compared to the examination under anaesthesia (EUA) staging methods?

1.5 OBJECTIVE

1.5.1 Main Objective

To compare the bedside and examination under anaesthesia staging methods for staging cervical cancer among suspected patients of cervical cancer at UTH.

1.5.2 Specific objectives

1. To compare the bedside and examination under anaesthesia staging methods for staging cervical cancer.
2. To identify factors that may limit bedside staging method for cervical cancer.

1.6 VARIABLES

1.6.1 Socio demographic variables

The socio-demographic variables of interest were age, marital status, education level, parity, history of previous clinical exam and HIV status

1.6.2 Clinical variables

The clinical variables studied were urine macroscopic examination, speculum examination, bimanual and recto-vaginal examination and patient related factors. Patient related factors were used to study the limitation associated with bedside clinical staging method.

The macroscopic urine examination based on appearance were described as clear, cloudy or hematuria (blood stained).

Speculum examination for macroscopic cancer lesions on the cervix and /or vaginal. The lesion macroscopic size and spread variate were 4cm and less, more than 4cm, and cancer spread beyond the cervix to up to / or upper two third vagina or lower third of vagina**.**

The bimanual and recto-vaginal examination of the pelvis for evidence of cancer spread to the parametrium and other surrounding pelvic structures. Variable of interest were parametrium spread described as thin, thick allowing uterine mobility, and fixed to pelvic wall allowing little or no uterine mobility.

Digital rectal palpation for cancer spread to the rectum.

The variable of interest on patient related factors during cervical cancer staging performed on bedside clinical staging method were patient cooperation, pain, pelvic tightness and bleeding. Quantification of these variables can be subjective but for the purpose of this study haemorrhage of 50ml and less were graded as mild, above 50ml to 250ml as moderate and above 250mls as severe.

Table1: Types of Variables

Dependent Variable			**Variates**
1	Cancer stage	Categorical (Ordinal)	1b, 2a, 2b, 3a, 3b, 4
Independent Variables			
	Demographic Variables		
1	Age (Year)	Continuous	15 to 85
2	Marital status	Categorical	Single, Married, Divorced, Widowed
3	Education level	Categorical	None/Primary, Secondary, Tertiary
4	HIV status	Categorical	Negative, Positive
5	HIV treatment status	Categorical	Not on HAART, On HAART
	Clinical variables		
1	Urine examination (macroscopic appearance)	Categorical	Clear, Cloudy, Hematuric
2	Speculum examination (Cervical and vaginal spread)	Categorical (ordinal)	• 4cm or less lesion on Cervix, • More than 4cm lesion on Cervix, • Lesion spread up to/or upper 2/3 vagina, • Lesion up to lower 1/3 vagina
3	Bimanual examination (Parametrium and pelvic spread)	Categorical (ordinal)	• Thin, • Thickened, • Fixed to pelvic wall

4	Rectal examination (Rectal spread)	Categorical	Mobile, Tethered
5	**Patient related variables**		
5(I)	Cooperation	Categorical	• Good (patient allows examination in a freely relaxed manner) • Poor (patient examined under struggle)
5(II)	Pain	Categorical	Mild, Moderate, Severe
5(III)	Pelvis	Categorical	Relaxed, Tight
5(IV)	Bleeding	Categorical	• Minimal (less than 50ml loss), • Moderate (above 50 to 250mls loss), • Severe (Above 250mls loss)

For the purpose of this study, radiologic examinations, chest x-ray, and ultrasound did not form part of the patient assessment for involvement of the ureters for stage 3b and distant metastases to the liver or lungs for stage 4b. The assessment for the two staging method were the same. Patients with pelvic wall spread clinically were staged as 3b and those with cancer spread beyond pelvic wall as only 4.

CHAPTER TWO

REVIEW OF LITERATURE

The literature review on the cervical cancer staging methods was conducted to determine the amount of knowledge on the bedside clinical staging method and pre-existing knowledge on cervical cancer staging method performed on examination under (general) anaesthesia (EUA).

There was a wide knowledge gap on the bedside staging method for cervical cancer and most of the information accessed was on examination under general anaesthesia (EUA) clinical staging method for cervical cancer. The international Federation of Gynaecology and Obstetrics (FIGO) defines cancer staging as the expression of the extent of cancer spread, whose main purpose as internationally agreed, is to offer a classification of the extent of cancer spread as the method of conveying one's clinical experience to others for purpose of comparison of treatment methods without confusion and ambiguity (Pecorelli and Odicino, 2003). According to Creasman (1995), the FIGO clinical staging system is for the purpose of comparison only and not for guiding therapy (Schilder and Stehman, 2003; Moore, 2006) and is the most prognostic factor for cervical cancer (Park and Soshio, 2009).

The original cervical cancer staging system based on clinical examination was introduced in 1928 by the League of Nations and seven revision modifications made between 1950 and 1994 by FIGO, the current patron of the system (Mutch, 2009). However, despite these modifications to cervical cancer staging system, debate and controversies has continued like clinical staging versus surgical staging, staging performed under general anaesthesia (EUA) versus bedside. Cystoscopy, sigmoidoscopy, intravenous pyelography examinations are now considered optional and not mandatory during the staging of cervical cancer (Mutch, 2009).

The clinical staging system for cancer of the cervix advised by FIGO is through bimanual palpation and speculum examination with or without additional investigation of cystoscopy, proctoscopy, or MRI where available. However, in many low resources setting, the most feasible approach to clinical staging is through a speculum examination for vaginal and cervical lesion, and bimanual palpation of the vagina and rectum (Sellar and Sankaranarayanan, 2003).

The FIGO clinical staging system for cervical cancer disease is I to IV, classifying the cancer disease into early and advanced disease. Stage 1 to 2A is classified as early cervical cancer disease and 2B to 4B as advanced disease (Moore, 2006; Schorge et al., 2008*)*. Stage I disease is a cancerous growth localized to the cervix and is divided into substages 1A and 1B. Stage IA is micro-invasive cancer limited to stromal invasion with maximum depth of 5mm and no wider than 7mm in diameter (Sankaranarayan and Wesley, 2003*)*. Stage IA cervical cancer is histological diagnosed. Cancer of the cervix stage IB through IV disease is macroscopic and allows for clinical staging.

Stage I disease is confined to the cervix, stage II is spread from the primary site to the upper vagina or parametrium divided into IIA and IIB. Stage IIA disease is spread to the upper two third of the vaginal while IIB is spread to the parametrium tissue. Stage III disease is further spread of the cervical cancer to lower third of the vagina and/or to the pelvic walls, divided into IIIA and B. Stage IIIA is spread to the lower third of the vagina and IIIB is spread to the pelvic wall and/or involvement of the ureter or hydronephrosis. Stage IVA is spread to surrounding pelvic organs while IVB is distant metastasis (Sankaranarayan, 2003).

Table 2: FIGO clinical staging for cervical cancer

0	**Carcinoma in situ**	
I	**Cervical cancer confined to cervix**	
	IA	Microscopic lesion (Histology diagnosis)
	IA1	Stromal invasion ≤3mm depth and ≤7mm in horizontal spread
	IA2	Stromal invasion >3mm and ≤5mm with horizontal spread ≤7mm
	IB	Clinically macroscopic lesion confined to the cervix
	IB1	Clinical lesion ≤4.0 cm in greatest dimension
	IB2	Clinical lesion >4.0cm spread in greatest dimension
II	**Cervical cancer spread beyond the uterus but not to pelvic wall or lower third of vagina**	
	IIA	No parametrium invasion IIA1 clinical lesion ≤ 4.0cm in greatest dimension IIA2 clinical lesion >4.0cm in greatest dimension
	IIB	Parametrium invasion
III	**Cervical cancer extends to pelvic wall or lower vagina /and or cause hydronephrosis or non-functioning kidneys**	
	IIIA	Cervical cancer involves lower third of vagina without extension to pelvic wall
	IIIB	Cervical cancer extends to pelvic wall and /or causes hydronephrosis or non-functioning kidney
IV	**IVA**	**Cervical cancer invades mucosa of bladder or rectum and/or extends beyond true pelvis**
	IVB	**Distant metastasis**

Adopted from "Staging Classifications and Clinical Practice Guidelines for Gynaecologic Cancers" by JL Benedet, S. Pecolli et al. 2000, with minor modifications.

The FIGO cervical cancer clinical staging system recommends that staging should be based on the best available knowledge at hand and changes to the system should only be made over time based upon development or acquisition of new knowledge. According to FIGO, one of the characteristics of a good staging system is its suitability for day to day use in a wide range of clinical environments and should have readily available diagnostic procedures that can be used by most clinicians (Pecorelli et al., 2000). Staging systems should be evidence-based and user-friendly should be based on and updated according to the latest available knowledge, implying that cancer staging systems should be responsive and adaptive to scientific development (Odicino et al. 2008).

The current FIGO clinical staging for cervical cancer revised in 2006 recommends that clinical staging be performed by an experienced examiner (clinician). However, the clinical staging of cervical cancer even in experienced hands has shown inaccuracy of 40 to 60 percent in assessing the parametrium involvement as observed by research findings even when performed on examination under anaesthesia the gold standard where patient and pelvic muscle are relaxed (Odicino et al., 2001; Eifel et al.,2009). Studies have revealed varying clinicians parametrium thickening interpretation without nodularity and further noted that early vaginal involvement may be difficult to diagnose accurately on the basis of pelvic examination even under experienced hands even in cases performed on examination under general anaesthesia (Eifel et al., 2009). It can be argued that examination under anaesthesia alone does not contribute to accurate staging of all cases but other factors, like clinician's experience, has an influence on the accuracy of the clinical staging of cervical cancer.

Cervical cancer staging performed under cooperation by an experienced clinician with only speculum examination and bimanual palpation can often provide sufficient information for successful staging (WHO, 2006). This requires absence of doubt, a patient that is not too tense and with minimal pain. The examination under anaesthesia is desirable as it removes doubt, the tension in the patient and pain. Odicino et al (2008) made the following statement "As scientists responsible for maintaining, modifying, and proposing changes to the existing staging systems, we indeed feel we shoulder an enormous responsibility to make the appropriate changes timely, wisely, and based on sound scientific data." This statement supports the argument that a change of staging method to the bedside method should be embraced by clinicians should scientific data through research show it to be equivalent.

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study design

Prospective cross sectional study

3.2 Study setting

The department of Obstetrics and Gynaecology at the University Teaching Hospital (UTH). UTH is the largest tertiary hospital in the country and shares ground with two institutions involved in cervical cancer management; the cervical cancer screening clinic in the Adult Infectious Disease Centre (AIDC) building and the Cancer Diseases Hospital (CDH) which is the only cancer hospital in the country. The department of obstetrics and gynaecology conducts outpatient gynaecology clinics Monday to Friday afternoon and under five different Units (Firms A, B, C, D and E).

The department has two gynaecology in-patient wards – C01 and C02, and its own Obstetrics and Gynaecology operating theatre. The elective cases, including suspected cervical cancer cases for examination under anaesthesia, biopsy and staging are performed from Monday to Friday by different Firms.

3.3 Target population

Suspected cervical cancer patients seeking EUA, biopsy and staging at University Teaching Hospital.

3.4 Study population

All suspected cervical cancer patients scheduled for examination under anaesthesia, biopsy and staging that meth the eligibility criteria (after administering inclusion and exclusion criteria).

3.5 Sample size calculation

The department of Obstetrics and Gynaecology performed 610 cases of cervical cancer staging examined under general anaesthesia in 2010. Using 610 at 95% proportion of the expected frequency of new cases, at 95% Confidence level and

confidence limit of 5%, using the epi info version 7 employing a single proportion formula the sample size of 65 was calculated.

3.6 Sampling method

A non-probability convenience sampling method was used to select study participants. The sampling method was employed because of the limited number of study participants meeting the criteria

3.6.1 Inclusion criteria

1. Suspected cervical cancer cases scheduled for examination under anaesthesia (EUA), biopsy and staging
2. Participants with a written consent

3.6.2 Exclusion criteria.

1. Post radiotherapy old cervical cancer cases referred from Cancer Disease Hospital
2. Participants declining to consent to participate.

3.6.3 Study duration

The study was conducted over a period of 5 months with the first participant recruited in December 2013 and last in April 2014.

3.7 Data collection tool and technique

A standardized checklist with variables of interest was used to collect desired data on social demographic and clinical variable. A paired test data collection technique defined as two tests applied to each participant was used to collect data. This reduces variability in making comparison between tests by eliminating between participant variance. The conditions to be met for the paired test data are; (1) result of one test should not interfere with the other, (2) conditions under which the tests are performed should not differ systematically, (3) the test should be performed without the knowledge of the other (Alonzo et al., 2002).

The patients suspected of cervical cancer and scheduled for EUA, biopsy and staging on the theatre list were subjected to bedside staging method on the ward or outpatient clinic on day one before taken to theatre the following day two for

examination under anaesthesia staging method. Clinicians performing the staging as EUA were at the level of Registrar, Senior Registrar and Consultant Gynaecologist and were blinded from the results of the bedside staging method. A Registrar for the purposes of this study was defined as a postgraduate student at the level of second year and above working under the direct supervision of the Consultant gynaecologist. The results from each staging method were not communicated between the two clinicians involved in staging the same participant.

During each staging method, the following was done: bladder was emptied, speculum, bimanual and per rectal examinations. A light source, Sims speculum, and urinary catheter were used. Other materials were examination groves and swabs for packing in case of haemorrhage.

The staging procedure was discontinued in participants who complained of severe pain or failed to cooperate during the bedside staging method.

A standardized checklist coded with patient medical number for matching was completed during each staging method. The data collected was checked for completeness before entered for analysis.

3.7.1 Pilot study

A pilot study was conducted on five participants to test the instrument for reliability and validity. Minor modifications to the checklist on question 6 were made to restrict options "HIV positive status" to not on HAART or on HAART because all HIV positive patients with cervical cancer regardless of the CD4 count are suppose to be on HAART.

3.7.2 Data quality control

The checklist was edited for completeness and data not meeting the set standard was not entered for analysis.

3.8 Data analysis

SPSS version 17.0 statistical package was used to enter and analyse data. The data was presented in tables and graphs. Sensitivity test was calculated to show the

ability of the bedside staging method to stage cervical cancer correctly. Correlation coefficiency was calculated to show how the bedside staging method correlated to examination under anaesthesia staging method - the gold standard method of staging cervical cancer.

A clinical test is used to confirm or refute the presence of a disease or further the diagnosis process, thus a test is supposed to identify patients with the disease correctly or without a disease correctly (Lalkhen and McCluskey, 2008). The accuracy of a dichotomous screening test is quantified by comparing the results of the test with a gold standard definitive test for a disease (Alonzo et al., 2002). The accuracy of the bedside staging method in staging cervical cancer in this study was compared to EUA staging method - the gold standard staging method.

The True positive rate (TPR) also called the sensitivity is the proportion of patient with a disease and a positive test. For purpose of this study, the True positives were defined as bedside cervical cancer stages with the same stage as in comparison with the gold standard examination under anaesthesia cervical cancer stage.

The False positive rate (FPR) which is (1-specificity) is the proportion of patients with no disease but with a positive test. For purpose of this study, these were defined as bedside staged cervical cancer cases over staged.

False negative (FN): proportion of patients with the disease but with a negative test. These in this study were defined as cases of bedside staged cervical cancer cases under staged.

The True negatives (TN): patients without a disease with a negative tested

The results were presented in a 2 X 2 contingency table. The sensitivity, Positive Predictive Value (PPV) of the test and the likelihood ratio were calculated from this table.

A 2 x 2 contingency table for calculating sensitivity, positive predictive value accuracy and specificity

Staging method	EUA (Gold standard)	
Bedside	TP (Correct staged)	FP (Over staged)
	FN (Under staged)	TN

Sensitivity is defined as the ability of the test to correctly identify those patients with the disease and for the purpose of this study will be define as the ability of the procedure to correctly identify those cases of cervical cancer staged using bedside staging method correctly calculated using the formula : Sensitivity= TP / (TP + FN).

The Positive Predictive Value (PPV) of a test is defined as the proportion of how likely is a patient has the disease given that the test result is positive, which will be define as the proportion of cancer of the cervix staged using the bedside staging method accurately staged calculated as PPV = TP/ (TP + FP).

The likelihood ratio is defined as the likelihood of a patient with a positive test has a disease compared to one with negative test, calculated as = Sensitivity/ (1-specificity)

3.9 Disseminations of the study findings

The study findings were disseminated to the department of Obstetrics and Gynaecology, Postgraduate students, Academic staff from other disciplines, Clinicians and Policy makers during public defence. It is further anticipated to be submitted for publication in local and international journal for peer review.

3.10 Ethical considerations

The study approval was provided by the Department of Obstetrics and Gynaecology and the Graduate Proposal Presentation Forum. Written permission to conduct the study was obtained from University Teaching Hospital management institution through the Senior

Medical Superintendent. The ethical clearance was done by ERES CONVERGE IRB Ethics Research Committee.

The exposure of participants to two staging methods as opposed to one method-examination under anaesthesia (the gold standard for staging the cervical cancer) could cause anxiety, stress, and psychological trauma to patients who were already traumatized from the experiencing of being suspected of having cervical cancer. The bedside staging method further subjected participants to the potential of discomfort, risk of varying degree of pain and bleeding from the cervix on contact. The benefits were to future patients.

The written consent was obtained from participants after giving them information on study benefits, risks and an assurance not to deny them treatment should they feel not ready to take part. Treatment of pain in form of analgesia, and patient were counselled on blood transfusion in case of severe haemorrhage resulting from contact bleeding during bedside staging. No blood samples or human tissue specimens were collected for this study except for the purpose of transfusion in case of severe haemorrhage. This was not for research purposes but as standard of care.

There was no money or gifts that were given participant to induce them to participate in the study except for the information on their disease condition.

CHAPTER FOUR

4.0 RESULTS

The sample size for the study was 65 but only 23 participants were recruited because of the challenges arising from the system, which will be discussed under the study limitations.

4.1 Socio-demographic variable

The socio-demographic variables that were studied obtained included age, marital status, education status and, HIV and the treatment status.

The age ranged from 34 to 79 years with a mean age of 51.6 years.

The majority of the participants were either divorced or widowed, both representing 30 percent respectively of all participants.

The majority of the participants (87 percent) had no form of education or had only some primary education. Most of the participants were HIV negative (52 percent) and of those that were HIV positive, 90 percent were on HAART.

Table 3: Socio- demographic variables by frequency and percentages

Variable	Frequency	Percent
Marital status (n=23)		
Single	2	8.7
Married	6	26.1
Divorced	7	30.4
Widowed	7	30.4
Education (n=23)		
No/primary	20	86.9
Secondary	3	13.0
Tertiary	0	0.0
HIV status (n=23)		
Negative	12	52.2
Positive	9	39.1
Unknown	2	8.7
Age in years (n=23)	**Frequency**	**Percentage**
Below 35	2	8.7
35 to 54	13	56.5

4.2 Clinical variables

The clinical variables that were studied on comparison of the two staging methods (bedside and EUA) are urine appearance, speculum examination, bimanual examination and rectal examination and the staging assigned.

Table 4: Frequencies and percentages of speculum examination results from EUA and bedside staging methods

Examination	EUA		Bedside	
	Frequency	**Percent**	**Frequency**	**Percent**
Speculum examination for progressive cervical cancer lesion	(N=23)		(N=23)	
4cm size or less on the cervix	1	4.3	2	8.7
Larger than 4cm on the cervix	5	21.7	5	21.7
Spread to upper 2/3 vagina	11	47.8	9	39.1
Spread to lower 1/3 vagina	5	21.7	6	26.1
Other findings	1	4.3	1	4.3

Table 5: Cross tabulation table for speculum examination results for EUA and bedside staging methods

Staging Method		EUA (Gold standard)					
	Speculum examination for progressive cervical cancer lesion	4cm size or less on the cervix	Larger than 4cm on the cervix	Spread to upper 2/3 vagina	Spread to lower 1/3 vagina	Other findings	**Totals**
Bedside	4cm size or less on the cervix	1	0	1	0	0	**2**
	Larger than 4cm on the cervix	0	3	2	0	0	**5**
	Spread to upper 2/3 vagina	0	1	8	0	0	**9**
	Spread to lower 1/3 vagina	0	1	0	5	0	**6**
	Other findings	0	0	0	0	1	**1**
	Totals	**1**	**5**	**11**	**5**	**1**	**23**

Pearson coefficiency correlation for the speculum examination from the two methods at *95% CL* was 0.738

Pearson coefficient correlation (r) can be calculated using the formula below

$$= \frac{\sum X^2 + \sum Y^2 - \sum d^2}{2\sqrt{\sum X^2 \times \sum Y^2}}$$

$\sum X^2$ = summation of the mean score of X

$\sum Y^2$ = summation of the mean score of Y

$\sum d^2 = \sum (X-Y)^2$

Adopted from statistical methods concepts, application and computation (YP Aggarwal; 2002)

Sensitivity and accuracy of the speculum examination during bedside staging

TP (Correct findings) 18, FP (exaggerated findings) 3, FN (under exaggerated) 2, TN 0

Sensitivity = TP/ (TP + FN) = 18/ (18 + 2)

= 0.9 = **90%**

Accuracy = TP / TP +FP + TN + FN) = 18 / (18 + 3 + 0 + 2)

= 0. 78 = **78%**

Table 6: Cross tabulation table for bimanual examinations findings during EUA and bedside staging method

Staging Method		**EUA (Gold standard)**			
	Bimanual examination for progressive cervical cancer spread to parametrium/pelvic wall	No spread to parametrium (Thin)	Spread to parametrium (Thick)	Spread to pelvic wall	**Totals**
Bedside	No spread to parametrium (Thin)	5	1	0	**6**
	Spread to parametrium (Thick)	3	1	0	**4**
	Spread to pelvic wall	0	4	9	**13**
	Totals	**8**	**6**	**9**	**23**

Pearson coefficiency correlation for the bimanual examination from the two methods at *95% CI* was 0.810

Sensitivity and accuracy of the bimanual examination during bedside staging

TP (Correct findings) 15, FP (exaggerated findings) 1, FN (under exaggerated) 7, TN 0

Sensitivity = TP/ (TP + FN) = 15/(15 + 7)

= 0.68 = **68%**

Accuracy = TP / TP +FP + TN + FN) = 15 / (15 + 1 + 0 + 7)

= 0. 65 = **65%**

Table 7: Cross tabulation table for per rectal examinations results on EUA and bedside staging methods

Staging Method		**EUA (Gold standard)**		
	Per rectal examination for cervical cancer spread to the rectum	No spread to the rectum (mucosa free and mobile)	Spread to rectum (mucosa tethered/ adherent)	**Totals**
Bedside	No spread to the rectum (mucosa free and mobile)	21	0	**21**
	Spread to rectum (mucosa tethered/adherent	0	2	**2**
	Totals	**21**	**2**	**23**

Table 8: Cross tabulation table for assigned cervical cancer stages by EUA against bedside methods

Staging Method		EUA (Gold standard)							
	cervical cancer stage assigned	**1B**	**2A**	**2B**	**3A**	**3B**	**4**	**No Cervical cancer**	**Totals**
Bedside	**1B**	0	0	0	0	0	0	0	**0**
	2A	0	2	1	0	0	0	0	**3**
	2B	0	3	2	0	0	0	0	**5**
	3A	0	0	1	2	0	0	0	**3**
	3B	0	0	1	1	3	1	0	**6**
	4	0	0	0	0	1	3	0	**4**
	No CaCx	0	0	0	0	0	0	2	**2**
	Totals	**0**	**5**	**5**	**3**	**4**	**4**	**2**	**23**

The Pearson coefficiency correlation between the two methods at *95% CI* was **0.929**

The sensitivity, positive predictive value and accuracy of the bedside staging method in staging cervical cancer

For the purpose of this study, to calculate the sensitivity and the positive predictive value of bedside staging method the true positive (TP) are those that were accurately staged in comparison to the EUA staging method. False positive (FP) are cases that were over staged, False negatives (FN) are cases that were under staged and the true negatives (TN) are cases that were suspected of having cancer but found no cancer on staging.

The cases that were correctly staged were 14, over staged cases 7, under staged 2 and found with no cancer 2.

Staging method	**EUA (Gold standard)**	
Bedside	TP (14)	FP (7)
	FN (2)	TN (2)

Table 9: Comparing the EUA assigned stage to the bedside assigned stage.

Stage	EUA stage assigned	Correct staged by Bedside (%)	Under staged by bedside (%)	Over staged by bedside (%)
1B	0	0	0	0
2A	5	2 (40.0)	0 (0.0)	3 (60.0)
2B	5	2 (40.0)	1 (20.0)	2 (40.0)
3A	3	2 (66.7)	0 (0.0)	1(33.3)
3B	4	3 (75.0)	0 (0.0)	1 (25.0)
4	4	3 (75.0)	1 (25.0)	0 (0.0)
No CaCx	2	2 (100)	0 (0.0)	0 (0.0)
Total	**23 (100)**	**14 (61.9)**	**2 (8.7)**	**7 (30.4)**

The sensitivity of the bedside staging method

Sensitivity = $\frac{\text{TP(Correctly staged)}}{\text{TP (Correctly staged) + FN (understaged)}}$

= 14/16 = 0.875 = **87.5%**

The positive predictive value of the bedside staging method

PPV = $\frac{\text{TP(Correctly staged)}}{\text{TP (Correctly staged) + FP (Over staged)}}$

= 14/ (14 + 7) = 14/21 = 0.67 = **67%**

The accuracy of the bedside staging method for cervical cancer staging

Accuracy = $\frac{\text{TP(Correctly staged) + TN(No cancer)}}{\text{TP (correctly staged) +FP (over staged) +FN (under staged) + TN (No cancer)}}$

= (14 +2) / (14 + 7 + 2 + 2) = 16/25 = 0.64 **= 64%**

Patient-related factors that may influence the bedside staging methods

The variables that were assessed are cooperation, pain, bleeding and pelvic muscle tightness. These were cross tabulated with the allotted cervical cancer stages assess whether their effect was statistically significant at $P \geq 0.05$

Table 10: Cross tabulation table of patient related factors versus cervical cancer stages assigned by bedside method

Variable	Cervical cancer stage allotted by bedside staging method							TOTALS	*P-Value*
		2A	**2B**	**3A**	**3B**	**4**	**No cancer**	**Frequency (%)**	
Cooperation (n= 23)	Full	3	1	1	4	1	2	**12 (52.2)**	***0.870***
	Difficulty	0	4	2	2	3	0	**11 (47.8)**	
Pain (n = 23)	Mild	2	1	1	2	0	2	**8 (34.8)**	***0.826***
	Moderate	1	0	2	3	1	0	**7 (30.4)**	
	Severe	0	4	0	1	3	0	**8 (34.8)**	
Bleeding (n = 23)	Mild	2	2	0	4	1	1	**10 (43.5)**	***0.217***
	Moderate	1	3	3	1	2	0	**10 (43.5)**	
	Severe	0	0	0	1	1	0	**2 (8.7)**	
Pelvic muscle (n=23)	Relaxed	3	2	3	5	2	2	**17 (73.9)**	***0.913***
	Tight	0	3	0	1	2	0	**6 (26.1)**	

Most patients (52.2 percent) cooperated during the bedside staging against 47.8 percent who had difficulties to be examined *(p- value 0.870) at 95% CI.* About one third (1/3) of the patients had complained of either mild, moderately or severe pain respectively during evaluation on bedside staging method *(p- value 0.826) at 95% CI.* Majority of the patients

(73.9 percent) were pelvic muscle relaxed during evaluation on bedside staging method *(p-value 0.913) at 95% CI.* Most of the patient had minimal or moderate bleeding (43.5 percent respectively) during the evaluation speculum and bimanual examination *(p- value 0.217) at 95% CI.*

CHAPTER FIVE

5.1 DISCUSSION OF FINDINGS

The analysis was based on the 23 cervical cancer patients who met the eligibility criteria. The study sample of 65 could not be reached because of the constraints and limitations. Because of human resource challenges, the theatres were operating at a minimal capacity and restricted to major cases and emergencies. This is the very argument that was being forwarded to allow for bedside staging methods rather than EUA, which is dependent on the theatre usage.

The mean age for the participants was 51.6 years, consistent with 50 years in most of other cervical cancer studies findings (Lai et al 2007). Most of the patients of cervical cancer have a low social status with low education status documented in most studies, Lui et al (2012) in a cervical cancer related study conducted in Lusaka found the majority of women with a mean education years of 8.3 +/- 3.6 years, which is just some primary education as this study revealed. Eighty seven percent of the participants had no or primary education similar to the study done in South Africa where low or no education was associated with late presentation of cervical cancer. The majority of these women were widowed or divorced. The study did not explore the reasons leading to divorce or widowhood but one patient revealed that she was divorced because she could not offer her husband sexual encounter whenever requested due to pain and bleeding she experienced each time they had sex.

Nearly all the patient who were HIV positive were on HAART and invasive carcinoma of the cervix (ICC) is one of the AIDS defining condition; HIV patients once diagnosed with cervical cancer are supposed to be initiated on HAART regardless of the CD4 count. The one patient not on HAART in the study had just presented and was being worked up for treatment.

According to the literature, the examination under anaesthesia staging method, cystoscopy, sigmoidoscopy, and intravenous pyelogram are now regarded as optional and not mandatory in the staging of cervical cancer (Pecorelli, 2009; Mutch, 2009). However, no published literature was found on bedside staging method comparing it to the EUA staging method. Studies on other staging methods like the imaging through use of MRI, CT scan have been compared to EUA method of staging and their sensitivity, positive predictive value and accuracy in staging cervical cancer determined (Jeone et al., 2012). Despite the

imaging method having high sensitivity and positive predictive value, their use is limited because of the cost and is not always available in most centres. Compared to the EUA staging method, the speculum examination, bimanual and per rectal examination during the bedside staging had a significant correlation to the one done during EUA staging method. The study found a correlation of 0.73, 0.81 and 1.00 for the speculum, bimanual and per rectal examination assessment processes respectively during bedside staging method as compared to during the EUA staging method. The sensitivity and accuracy of the speculum examination during bedside staging method was 90 and 70 percent respectively while bimanual examination had sensitivity and accuracy of 68 percent and 65 percent respectively. This shows that the speculum examination during bedside staging method was able to pick as much clinical information as during EUA when the patient is relaxed.

The bimanual examination however, during bedside staging method, showed a low sensitivity and accuracy in assessing the cervical cancer spread to the parametrium and pelvic region. Similarly, studies have documented a lower sensitivity and accuracy of the bimanual examination during EUA even in the hands of experienced clinicians compared to when MRI assessment is employed. The inaccuracy of about 40 to 60 percent on clinical assessment has been documented by studies compared to MRI with a higher sensitivity in detecting parametrium involvement and tumour size (Odicino et al 2001; Eifel et al. 2009). Clinicians can vary widely in their threshold to determine parametrial involvement and vagina tumour extension (Eifel et al. 2009) and this could explain the reduced sensitivity and accuracy of the bimanual examination and should not be the basis to consider bedside staging method to be inferior to EUA staging method.

Overall, the bedside staging method to assign the accurate stage of the cervical cancer had a correlation of 0.929 with the sensitivity, positive predictive value and an accuracy of 87.5 percent, 67 percent and 64 percent respectively. These figures compare well to the sensitivity, positive predictive value and accuracy of MRI and CT scan (Jeone et al., 2012). The State-of–the-Clinic- Science (SOTS) meeting, recommended and agreed that clinical examination must remain mandatory for staging and evaluation and not imaging (CT, MRI).

Despite further arguments that EUA adds little benefits to clinical examination (Trimble el al.2009) there are cases (stage 2A) that will still require to be restaged on examination

under anaesthesia for fear of over exposing the patient to over treatment that may prove to be associated with severe side effects. Further, it was 2A that had highest number of overstaging. Five (5) cases were assigned stage 2A by EUA method and three (3) out of five translating into 60 percent were over staged and this may have some implication on the patient.

Stage 2A is the cut-off point for surgical treatment, and for a higher stage above this, the treatment option is radiotherapy only. Over-staging a patient will expose the patient to over-treatment associated with unnecessary side effects like induced radiotherapy menopause where preservation of ovarian function in younger premenopausal women or retention of the more functional and pliable vagina for sexual function may be desired (Konar, 2013). The study findings of 60 percent over-staging at 2A suggest that patient staged on bedside with stage 2A should be further subjected to EUA staging for an accurate assigning of stage to avoid over treatment. Assessing of the parametrium even with EUA can is associated with 40 to 60 percent inaccuracy (Odicino et al 2001; Eifel et al. 2009) hence the proposal by investigator to subject stage 2A on bedside to further restaging on EUA.

The study looked at some of the factors that may limit the use of the bedside staging method in the clinical practice. These were directly related to patient cooperation resulting from pain, pelvic muscle tightness and bleeding though this may be provoked during both methods. All the factors assessed were found not to be statistically significant in limiting the bedside staging method. However, in clinical practice care need to be taken as the sample on which this is based was small. Just over half of the patients had difficulties to be examined. Pain in the cervical cancer patient may be somatic from injury to the tissues and or visceral from spasms of smooth muscle or neuropathic from the entrapped nerves. About 25 percent women with cervical cancer experience some form of moderate to severe pain everyday (Movva et al, 2009). However, pain and pelvic muscle tightness maybe subjective and different patients have a different threshold for pain. The study found a third of the patients complained of mild, moderately and severe pain respectively during evaluation on bedside staging. The majority of the patients (73 percent) were relaxed during pelvic examinations. Poor patient cooperation and tightness of pelvic muscle mostly due to fear and/or pain can greatly affect the results of the bedside staging. In fifty percent (50%) there was poor cooperation and more than sixty percent (60%) expressed moderate to severe pain. The author therefore suggest the use of some form of

anxiolytics and/or analgesia whenever the bedside method is employed in staging patients with cervical cancer to minimise or risk of affecting the staging result due to these patient related factors.

Bleeding from the cervical cancer lesion on minimal contact is a known complication among cervical cancer patients. This commonly occurs on staging the cancer on examination under anaesthesia method in theatre. This factor though considered patient related is disease related. The haemorrhage resulting from even minimal contact of necrotic tumour tissues can be life threatening (Movva et al, 2009). Cervical cancer patients seeing themselves bleed due to contact bleeding during the bedside staging method will induce fear and panicking leading to poor patient cooperation. It was difficult to make interpretation of bleeding as most patients with different cancer stages had bled either mildly, moderately, or severely. Patients with lower cancer stages of 2A to 3A bled mildly while severe bleeding was associated with very advanced cancer of the cervix stage 3B and 4.

5.2 CONCLUSION

Although the results discussed in this study are based on a small sample size they represent an opportunity for further clinical investigation on this important subject. The sample was not sufficient to recommend abandoning the standard clinical practice (EUA staging method) in staging cervical cancer patients for bedside though it has revealed some significant findings with a positive significant correlated of 0.9 to the standard (EUA staging) method. The bedside staging method under investigation had a high sensitivity of 87.5 percent, a positive predictive value of 67 percent and an accuracy of 64 percent. However, the bedside method was more often associated with over-staging than under staging of cases and this was more apparent with stage 2A. The clinical limitations arising from patient factors were not statistically significant thought this may not be conclusive due to the small sample size on which this was based.

5.2 STUDY CONSTRAIN/ LIMITATIONS

The analysis of the study was based on a small sample size, as the calculated study sample size could not be reached due to shortage of theatre staff leading to cancellation of cases of gynaecology surgical cases on the lists. The parametrial tissue involvement is clinically difficult to assess and studies comparing accuracy of clinical assessment with imaging

have documented this. It is clinician dependant to some degree and could have affected both arms of the results. The sample was collected from only one centre and due to these limitations results could not be generalized and taken as representative.

5.3 RECOMMENDATIONS

1. The study findings should be regarded as baseline findings for a future study that should compare the bedside staging methods to examination under anaesthesia (EUA) staging method with a representative sample size before the findings can be implemented into clinical practice.
2. The EUA method should continue to be employed in staging cervical cancer patients that are suitable for general anaesthesia. For patients suspected of cervical cancer with contraindications to anaesthesia, the bedside staging method is an option that should be employed after administration of either an anxiolytic and/or analgesia and should not be denied the clinical staging for the benefit of prognosis of the disease and treatment initiation
3. A large representative sample is needed for protocol formulation to guide patient selection criteria and the limitation of the bedside staging method in clinical practice.

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APPENDICES

APPENDIXA; PARTICIPANTS' INFORMATION SHEET

Introduction

I **Abby Makukula,** a Postgraduate Student in the Department of Obstetrics and Gynaecology, School of Medicine at the University of Zambia is kindly requesting for your participation in the study '***A comparative study of bedside and examination under anaesthesia clinical staging methods for cervical cancer at UTH in Lusaka, Zambia'*** where I am gathering data on the method of assessing the extent of cervical cancer spread, the condition you have. The purpose of this information sheet is to enable you understand what is involved and enable you make an informed consent should wish to participate in the study.

While taking part in this study or decline to participate, you will not be discriminated against or denied any information / services pertaining to the investigation and treatment of the cancer you are seeking. Your participation is voluntary and you are under no obligation to take part should you think otherwise. I will explain to you what will be involved while participating in this study and if you accept to take part, a form will be issued to sign or put a thumb print to show consent.

Purpose of the study

The purpose of this study is to gather information on the bedside and general anaesthesia clinical staging methods used to assess the extent of cervical cancer spread the condition you have for improving cancer services for future cervical cancer patients.

Procedure

If you consent to participate, you will have two separate clinical examinations to determine the extent of cervical cancer spread by our specialist doctors in gynaecology, in the ward or clinic on the first day and in theatre under general anaesthesia the following day. No blood, specimen will be collected for the purpose of this study except for cases of transfusion in case of excessive bleeding and for the purpose of knowing the type of cervical cancer you have.

Risks and discomforts

You will be examined twice for the evaluation of the cervical cancer spread- in the clinic or ward and in theatre the following day, with a possibility of causing you some stress. During evaluation in the clinic or on the ward, you may experience discomfort, pain, and/or bleeding. In case of pain, feel free to mention it to your doctor for painkillers.

Benefits

You will be privileged to know more about the cancer of the cervix you have by asking any question(s) related to it. Note that no monetary favours, gifts will be given to you for agreeing to participate in the study. The information will generate from the study will be disseminated to Clinicians and Policy makers to improve future cervical cancer services.

Confidentiality

All the information that will be collected during this study will be kept strictly confidential and only used for the purpose for this study and not any other. No name(s) will be written on the Checklist form except for the hospital number for the purpose of linking the findings. The Department of Obstetrics and Gynaecology at UTH or/and Research Ethics Committee from School of Medicine at UNZA may review the information that will be generated from this study but again it will be kept strictly confidential. The University Teaching Hospital Management and Department of Obstetrics and Gynaecology, the University of Zambia Research Ethics Committee that safe guards and protect the rights of the patient participating in clinical studies, have approved this study. In case of any ethical question(s) arising during your participation, feel free to contact the Chairman for the Research Ethics Committee and my study Supervisors on the address below.

CONTACT PERSON FOR ANY INFORMATION RELATED TO THE STUDY.

1. Principal investigator

   Dr Abby Makukula, Department of Obstetrics and Gynaecology, School of Medicine, University of Zambia, P.O. Box 50110, Lusaka. Cell: 097-7-748633, Email: abymak@gmail.com

2. Study Supervisor

   Dr M. Mwanahamuntu, Department of Obstetrics and Gynaecology, University Teaching Hospital, P.O. Box 50110, Lusaka. Cell: 0955887236, Email:

3. The Chairperson,
   ERES CONVERGE IRB, 33 Joseph Mwila Road, Rhodes Park, Lusaka, Telephone: 260-955 155 633/4, Cell: + 260-966 765 503, E-mail: eresconverge@yahoo.co.uk

PLEASE NOTE

1. Your participation in this study is entirely voluntary.
2. You are under no obligation to participate or continue in the study at any time should you otherwise feel so.
3. No monetary favours or gifts will be given for participating in the study.

Do you have any questions or clarifications to be made on what we have discussed?

CONSENT TO PARTICIPATE IN THE STUDY

I……..Hereby voluntarily CONSENT to participate in the study having been explained to in presence of a witness and understand the purpose of the study, procedure involved, risky/discomfort, benefits and confidentiality.

Sign/Thumb print …… Date……

Witness (Name)……. Sign……..

THANK YOU

APPENDIX B. CHECKLIST FOR DATA COLLECTING(Revised after pilot study)

A COMPARATIVE STUDY OF BEDSIDE AND EXAMINATION UNDER ANAESTHESIA CLINICAL STAGING METHODS FOR CERVICAL CANCER AT UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA

PARTICIPANT NUMBER…….. UTH FILE NUMBER……..

CLINICIAN STAGING PATIENT (a) Registrar (b) Senior Registrar/Consultant

BACKGROUND INFORMATION

1. Staging performed**:** (a) On bedside (b) Examination under anaesthesia (EUA)
2. Age to the nearest year (state)…….
3. Marital status (a) Single (b) Married (c) Divorced (d) Widowed
4. Education level (a) None /Primary (b) Secondary (c) Tertiary
5. HIV status (a) Positive [go to Qn6] (b) Negative (c) Not known
6. HIV positive (a) Not on HAART (b) HAART

CLINICAL ASSESSMENT

7. Urine appearance (macroscopic):
   (a) Clear (b) Cloudy or hematuric
8. Speculum examination for progressive cancer lesion:
   a) 4cm or less in size and confined to Cervix
   b) More than 4cm in size and confined to Cervix
   c) Spread to/or upper two thirds of vagina
   d) Spread to lower third vagina
   e) Others (Describe)……

9. Bimanual examination for progressive cervical cancer lesion:

   I. Parametrium: (a) Thin (b) Thick (c)Fixed to pelvic wall

   II. Others (Describe)……..

10. Per rectal examination:

(I) Free and mobile rectal mucosa (II) rectal mucosa tethered/adherent to tumour

11. **The patient related factors to be assessed during bedside clinical staging method only**:**[During general anaesthesia (EUA) clinical staging skip to Qn12]**

   I. Patient cooperation(a) Full cooperation(b) Cooperated with difficulties

   II. Pain (a) Mild (b) Moderate (c) Severe

   III. Pelvis (a) Relaxed (b) Tight

   IV. Bleeding (a) Minimal (b) Moderate (c) Severe

12. Final clinical cervical cancer stage assigned

a) 1B (b) 2A (c) 2B (d) 3A

(e) 3B (f) 4 (g) No Cancer (Other)

MAKE PATIENT COMFORTABLE AND THANK HER IF FULLY AWAKE