DETERMINANTS OF FACTORS AFFECTING ADHERENCE TO RADIOTHERAPY TREATMENT AMONG PATIENTS WITH CERVICAL CANCER AT THE M P SHAH HOSPITAL

BY

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DECLARATION

I declare that this dissertation research proposal is my own original work and that it has not been presented before either in whole or in part to this institution or any other institution elsewhere in the country for academic qualification.

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DEDICATION

I dedicate this project to my mother for her tireless efforts to see me make a breakthrough in the academic field. I owe a debt of thanks to the radiology staff at MP Shah Hospital; all my friends and colleagues and any other person who participated in the success of this study.

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I owe a debt of thanks to God for the provision of power of mind that gave me success in my pursuit of education. I also thank all my lecturers for their tireless effort in helping me carry out this research and especially my supervisor Prof.Mutuku A. Mwanthi and Dr.Chrisostim Barasa. Special thanks to all staff members for their immediate and genuine assistance whenever the need arose. I further extend my gratitude to the library assistants for their assistance and provision of relevant materials which aided the successful completion of this work.

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LIST OF ABBREVIATIONS

ACOG	American College of Obstetricians and Gynecologists
ASR	Age Standardized Rates
CBHI	Community Based Health Insurance
CT	Computed Tomography
EBRT	External Beam Radiotherapy Treatment
FIGO	International Federation of Gynecology and Obstetrics
GIT	Gastrointestinal Tract
GLOBOCAN	Global Cancer
GoK	Government of Kenya
HPV	Human papillomavirus
ISPOR	International Society for Pharmaoeconomics and Outcome Research
ICBT	Intracavitary Brachytherapy
KCBHFA	Kenya Community-Based Health Financing Association
KNH	Kenyatta National Hospital
KSHS	Kenya Shillings
LEEP	Loop Electrosurgical Excision Procedure
MRI	Magnetic Resonance Imaging
MV	Megavolt
NHIF	National Health Insurance Fund
PACT	Programme of Action for Cancer Therapy
PET	Positron Emission Tomographic
SEER	Surveillance Epidemiology and End Results
UoN	University of Nairobi
USD	United States Dollar
WHO	World Health Organization

ABSTRACT

Background: Cervical cancer is the second commonest cancer among women of reproductive age in Kenya. It has one of the highest incidences and mortality cases in Kenya.This is despite a lot of prominence being placed on preventive and screening services while there is a paucity of attention on the adherence of patients to the recommended radiotherapy treatment. Adherence to the recommended radiotherapy treatment sessions is vital for curative and prevention metastatic spread of the disease and reduction in mortality cases. Therefore, the aim of this study was to determine factors affecting adherence to radiotherapy treatment among patients with cervical cancer at the MP Shah hospital.

Methodology: This was a quantitative retrospective descriptive study. The study population consisted of all cervical cancer patients who underwent radiotherapy between January 2012 and January 2014 at the cancer center, MP Shah Hospital. Simple random sampling was used to select a sample size of 246 patients. A total of 20 patients were lost to follow up. The study employed the use of an electronic database. A structured close ended questionnaire was used to collect data and analysis was done using statistical package for the social science (SPSS) version 20.

Results: A high adherence rate was noted in patients within the 40-49 years age stratum. Marital status was a significant factor in explaining adherence to treatment with ($\chi 2$=4.945; df= 3 p=0.001) at bivariate level. The tertiary level of education showed significant association with adherence to treatment with ($\chi 2$=p.945; df= 3, p-0.002). Patients with stage two cervical cancer who were treated for less than 28 days and had less side effects were more adherent.

Conclusion and recommendations: This study showed that the most significant factors affecting adherence were having a tertiary level of education, being married; being within 40-49 years of age; early stage cervical cancer; being treated for not more than 28 days and having less side effects showed better adherence treatment. The recommendations of this study are: close monitoring of unmarried and divorced patients; with low levels of education and patients below the age of 39 years and above 60 years. Dose and treatment protocol optimization should be adopted and adapted. Further research studies should done to ascertain the reasons why certain age groups show high adherence to radiotherapy than others.

CHAPTER ONE: INTRODUCTION

1.1 BACKGROUND

Cancer is defined by the World Health Organization (WHO) as a group of diseases that can affect any part of the body. Most commonly used synonyms are tumors or neoplasms. The main characteristic feature of cancer is the uncontrolled cellular proliferation which spreads rapidly to other tissues and with resultant metastatic deposits to other organs. The metastatic spread of the disease is often a poor prognostic factor and cause of mortality from cancer (WHO, 2014).

According to Global Cancer database (GLOBOCAN) (2012), 14.1 million incidences of cancer and an estimated 8.2 million cases of cancer related mortality were recorded in 2012. This is compared with 12.7 million new cancer cases and 7.6 million deaths in 2008.By the year 2012, 32.6 million of the world's population had been diagnosed with a certain type of caner (GLOBACAN, 2012).

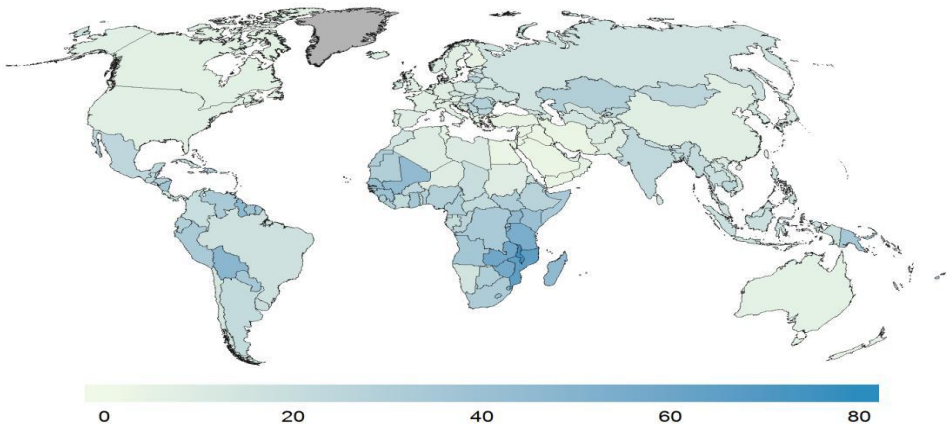


Figure 1: **An estimation of incidences of cervical cancer in 2012**

Source: (GLOBACAN 2012).

Cervical cancer begins from the cells of the cervix. It may begin from the mucosal cells of the cervix or from the glandular cells. In the commencement stage of the disease, cancerous cells proliferate within the cervix. As the disease progress, the cancerous cells invade adjacent organs and metastasize to other organs of the body (Ericka *et al*., 2012).

Histologically, squamous cell type is the commonest pathological diagnosis followed by adenocarcinoma cell type (Ericka *et al*., 2012).Controversy still persists on whether histological differentiation of cervical cancer is predictive of the disease spread or progression with some studies having shown that adenocarcinoma has a poor prognosis. However, other studies didn't find any correlation between the pathological type and malignant characteristics of cancer of the cervix (Yang *et al*., 2000).

There is overwhelming research evidence that cervical cancer is associated with human papillomavirus (HPV) as an etiological factor (ACOG, 2002). Other risk factors include: having coitus at an early age; having several coital partners; coital transmitted infections and cigarette smoking. Women with squamous dysplasias of the reproductive organs or retroviral disease are more susceptible to cervical cancer (Anttila *et al.*, 2001).

According to (Sankaranarayanan *et al.*, 2009), patients with no comorbidities, the HPV related infections will subside rapidly without causing clinically significant disease. Other non-clinical related factors such as low socio-economic status, long term oral contraceptive use, certain nutritional deficiencies and genetic susceptibility have been associated with an increased susceptibility of developing cervical cancer (Sellors & Sankaranarayanan, 2003).

Globally, areas with high prevalence rates include Eastern Africa, Melanesia, Southern and middle Africa while low prevalence areas in the world include Australia/New Zealand and Western Asia (WHO, 2014).The cases of mortality as a result of cervical cancer in 2012 were estimated at 266,000 deaths which represented 7.5% of all female patients diagnosed with cancer (GLOBACAN, 2012). Less developed countries have 87% of confirmed cervical cancer deaths globally as compared to developed regions. In other regions of the world, mortality range from less than 2 per 100,000 in Western Asia, Western Europe and Australia/New Zealand to more than 20 per 100,000 in Melanesia (http://globocan.iarc.fr.).

Africa has the highest incidences of cervical cancer and high age specific rates (WHO, 2014). Reports from the sub-Saharan Africa indicate that 34.8 per 100 000 women screened have cervical cancer with 22.5 in every 100 000 women dying as result of it (http://globocan.iarc.fr.). These figures are in contrast with reported rates in the United States of America of 6.6 and 2.5 cases in every 100 000 women, respectively (WHO, 2014). The sharp difference between Sub

Saharan Africa and North America age standardized rates can be attributed to inaccessibility to screening facilities in the former (Ferlay *et al*, 2013). East Africa and West Africa have a high incidence and mortality rates as compared to North Africa. For example, southern countries of Zambia, Malawi, Mozambique, and Tanzania have the highest incidence rate of 50 cases per every 100,000 people (GLOBOCAN, 2008).

In Kenya, cervical cancer is the second most common cancer among women with the highest mortality rate (National guidelines for Cancer Management Kenya, 2013).The annual reported cases of cervical cancer are 2454 with 1676 deaths. By the year 2025, it's projected that the number of new cervical cancer incidences will peak at 4261 (Kenya National Cancer Prevention Programme-Strategic Plan, 2012-2015).

Management of cervical cancer involves surgery, radiotherapy and chemotherapy or chemoradiotherapy. The modality chosen either for curative or palliative purposes is primarily dependent on the FIGO stage and patients comorbidities (WHO, 2014).

Surgery is usually used as a curative modality to resect the primary tumour. For early stage of lesions, conization, cryosurgery, laser surgery, or LEEP (loop electrosurgical excision procedure) are used for curative purposes (www.cancer.gov). These procedures are aimed at resection of the primary tumour without affecting the adjacent normal tissues. In cases of invasive carcinoma, radical hysterectomy is required to remove the uterus, cervix, and part of the vagina (www.cancer.gov).

Concurrent chemotherapy and radiotherapy has the advantage of achieving loco-regional control of the disease compared to radiotherapy alone. A retrospective meta-analysis of data from patients who were given concurrent chemoradiation for cervical cancer in 13 trials revealed a prolonged survival time for the patients (Quinn, 2006).

The standard chemotherapy dosage for cervical cancer involves an infusion of cisplatin once a week in 5–6 cycles. Studies show that this dosage has less toxicity and its more tolerable compared to combined dose of cisplatin and 5-fluorouracil in a 21-day schedule (Tae *et al*.,

2012). 5-fluorouracilbased regimens are an acceptable alternative for patients who are unable to access the standard regime. However, available information on the toxic levels and adverse effects as a result of chemoradiation are limited (Kim *et al.*, 2008).

Radiotherapy is the preferred modality of choice once the disease has metastasized from the primary site to other regions or when the tumor is unresectable (Hellebust et al., 2009). The management of cervical cancer with radiotherapy may often involve a combining external beam radiotherapy treatment (EBRT) and brachytherapy (John & Sankaranarayanan, 2003). The combination of EBRT and brachytherapy is associated with improved control of the disease, better prognosis and outcomes as opposed to EBRT alone. This is more important especially for locally advanced disease such as stage IIB and III (John & Sankaranarayanan, 2003).

Adherence to the recommended radiotherapy treatment sessions prevents local and regional spread of the disease (Sabate, 2003). This ultimately increases survival and remission of the disease. Hence, adherence becomes vital for better outcomes since radiotherapy plays an important role in the curative and palliative therapy of cervical cancer (William *et al*, 2007).

The International Society for Pharmaceutical Economics and Outcome Research (ISPOR) defined adherence as ‘‘the degree or extent of conformity to the recommendations about day-to-day treatment by the provider with respect to the timing, dosage, and frequency’’ (Kathryn *et al*, 2009). It further outlines that optimal adherence and persistence will happen when the patient complies with the recommended treatment (Sethi *et al*, 2010).

In this study, adherence will refer to the completion of the recommended radiotherapy treatment. Therefore, those patients who complete the recommended radiotherapy treatment will be deemed adherent. Non-adherence will refer to the patients who did not complete the recommended radiotherapy treatment because of some reasons (Ngugi, 2011).

The WHO has come up with a multifactorial model for adherence. It comprises of five factors which include: patient; treatment; disease; healthcare system and social economic related factors (Sabate, 2003). Some examples of socio-demographic and cultural factors include low

socioeconomic status, penury, illiteracy, joblessness, poor living conditions, inaccessibility to hospitals, cost of transport, expensive medication, dynamic environmental situations, cultural beliefs about diseases and family dysfunction (Ngondi, 2011).

Currently, over 85% of health costs in low income countries in Africa are paid in the form out of pocket mode. Out of pocket mode of payment doesn't provide financial risk protection. Hence, an estimated 100 million persons are being forced into penury every year because they lack insurance (PACT 2010). Due to lack of financial risk protection, adherence rate to recommended treatment is poor.

There have been relatively few research studies done on both the positive and negative effects of health system factors on adherence rates (WHO, 2003). It can be acknowledged that despite excellent patient provider relationship which may affect adherence positively, the persistence of the other factors have a detrimental effect on adherence (www.who.int). These factors include: poor service delivery; failure of insurers to reimburse hospitals; inefficient drug distribution systems; paucity of health educators and low motivation among health workers (WHO, 2003).Other systemic factors affecting adherence include lack of proper coordination, deficiency in mobilization of resources and poor service delivery, increased number of patients and poor staging of cancer (Lebeau *et al*, 2011).

Patient related factors such as illiteracy, misunderstandings, stress, depression, untoward effects of treatment, cultural and religious beliefs attempts to avoid negative side effects, phobia of cancer have a negative effect on adherence to recommended treatment. In other settings, studies have shown that lifestyle behaviors such as cigarette smoking and alcoholism have a detrimental effect on adherence to treatment (David *et al*., 2013).

Treatment and disease related factors have a notable effect on compliance to radiotherapy. Patients put on adjuvant chemo radiotherapy dose regiment are more likely to get haematological and gastrointestinal adverse effects. These untoward effects as a result of chemoradiotherapy dose regiment often lead to poor adherence rates. In addition, both the burden of the disease and the treatment adverse effects has a detrimental effect on the wellbeing of these women (Ying *et*

al., 2013).A research study which collected data from 177 cancer patients in Switzerland demonstrated that patients who had high adherence rates had fewer untoward effects due to treatment (Winterhalder *et al*., 2011).

1.2 STATEMENT OF THE PROBLEM

Adherence to radiotherapy treatment for patients with cervical cancer has received little attention in literature. Majority of the work that has been done has concentrated on challenges related to screening, treatment and its side effects, the disease process, and individual patient-related challenges. Few local studies have been done on adherence to radiotherapy treatment for cervical cancer.

So far the WHO has published four guidelines on cervical cancer management with much prominence put on screening for cervical cancerous lesions and management. None of these publications focuses on patient adherence to treatment as a means of reducing deaths resulting from disease progression due to poor compliance to the recommended treatment.

In Kenya, the policy makers have given gynecological cancers more attention and prominence. This is evident in the policy paper of reproductive health and the reproductive health strategic plan. The two strategic policy papers placed a greater prominence on health system strengthening in order to facilitate prevention, early diagnosis and proper palliative and curative therapy for cervical cancer (www.iedea-ea.org).

However, the two policy papers are silent on the adherence and non-adherence to the recommended treatment. Furthermore, they don't provide guidelines on how to improve or to ensure adherence to the recommended radiotherapy treatment in order to prevent recurrence and secondary spread of disease. Of note is the significant rise in the mortality rates of cancer of the cervix despite having a strategic policy in place. This makes it crucial to have a comprehensive study on patients' adherence to prescribed radiotherapy sessions. Poor adherence and early discontinuation of treatment may have a detrimental effect and affect the long term survival of patients.

Due to these difficulties, patients who don't adhere fully to the recommended treatment will not realize the benefits of radiotherapy. These may be manifested through poor local regional control of disease, progression of disease and increased cost as a result of prolonged hospital stay. By identifying the contributing factors to adherence, then it's possible to ensure patients comply fully with the recommended treatment which will lead to good outcomes.

1.3 JUSTIFICATION

The negative outcomes of not fully or not adhering to recommended treatment is associated with poor survival and high health related costs. Inadequate adherence has a negative impact on both the curative and palliative goals of treatment. Hence, the quality of life of patients and health economics of the nation are adversely affected. All efforts geared at enhancing adherence would result in favourable outcomes in extending and improving the quality of life of patients (WHO, 2014).

A lot of emphasis has been placed on preventive and screening strategies in the fight toward reduction of mortality due to cervical cancer. Treatment strategies also play a secondary role in the therapeutic management of cervical cancer. The purpose of this study was to identify factors affecting adherence to radiotherapy treatment among patients with cervical cancer.

The findings of this study may be integral for all the stakeholders either in the private sector or in government in order for them to formulate strategic plans or policy papers on adherence to treatment. In addition, it may help them in formulating strategies on how to deal with the factors affecting adherence rates within the health systems model.

CHAPTER TWO: LITERATURE REVIEW

2.1 INTRODUCTION

Cervical cancer continues to be one of the commonest causes of mortality in women of reproductive age. Estimates reveal that over a million women globally have been diagnosed with cancer of the cervix (GLOBACAN, 2012). Majority of these women lack accessibility to preventive, curative, palliative and rehabilitative health care services. In 2012, there were 528 000 new incidences of cervical cancer reported with a mortality rate of nearly 90% in low- to middle-income countries. If the current statistical figures continue to rise, mortality cases due to cancer of the cervix are likely to escalate by 25% by the year 2022 (WHO, 2013).

In the developed countries, Central and South America, South and South-East Asia, and the Western Pacific have reported high incidences of cervical cancer. However, the incidences of cervical cancer in the developed world have reduced largely due to availability of screening and treatment programmes. In contrast, rates in most developing countries have risen or remained static. Major disparities also exist in the developed world, where rural and poorer women are at greatest risk of invasive cervical cancer (WHO, 2013).

In developing countries, cancer of the cervix has a detrimental effect on the health and life of women. It remains the commonest cancer with the highest mortality rates in women of reproductive health. An estimated 500,000 incidences of cervical cancer are being reported annually with the bulk (80%) of the cases occurring in the developing countries (Chirenje, 2007).

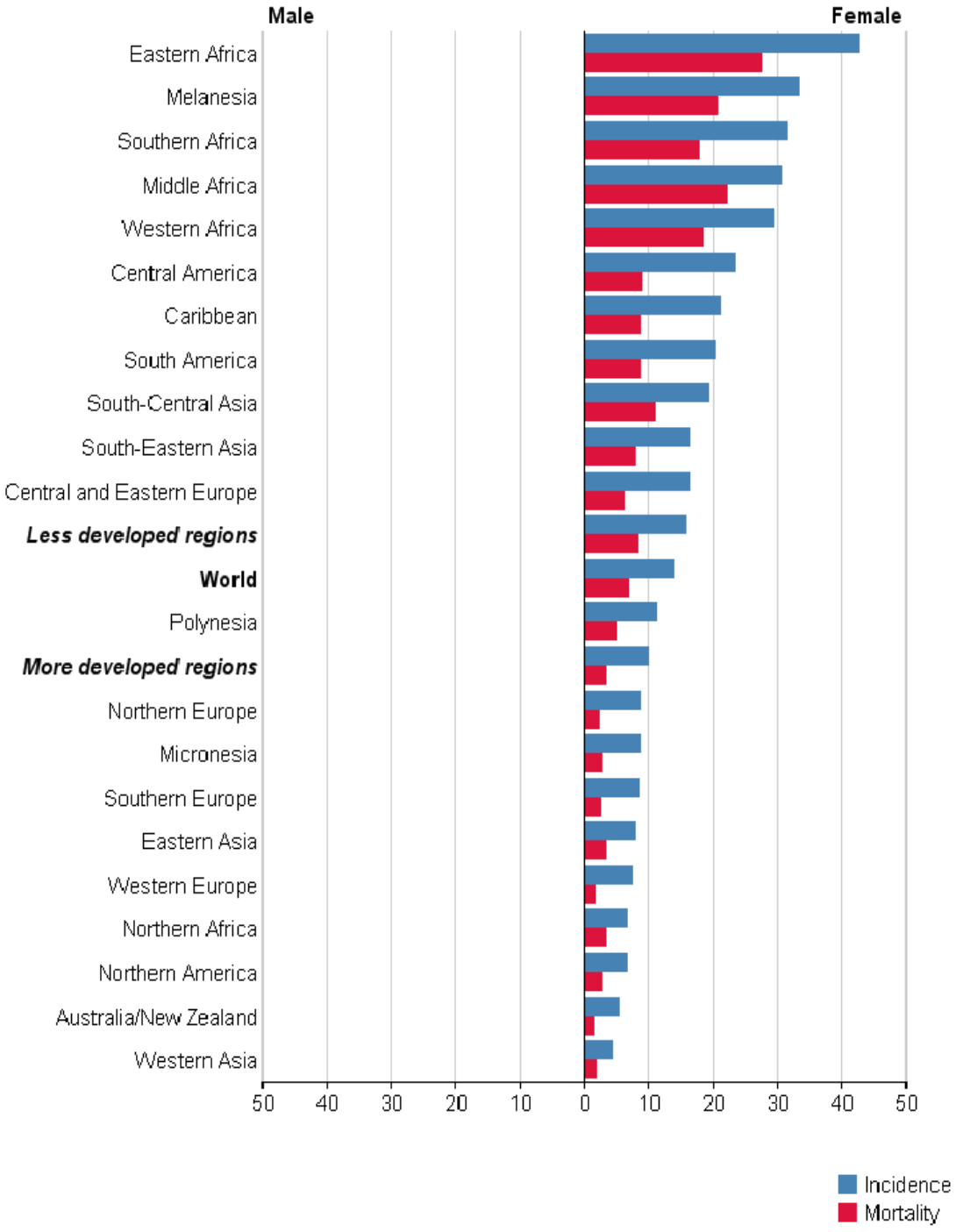


Figure 2: **Incidence and mortality rates of cervical cancer worldwide.**

Source: GLOBACAN 2012

Africa has the highest incidences of cervical cancer and high age specific rates (WHO, 2014). Reports from the sub-Saharan Africa indicate that 34.8 per 100 000 women screened have cervical cancer with 22.5 in every 100 000 women dying as result of it (http://globocan.iarc.fr.). These statistics are high as compared with 6.6 new cases per 100 000 and 2.5 cases per 100 000 mortality cases in North America. The difference can be attributed inaccessibility to screening facilities in least developed countries (Ferlay *et al*, 2013).

The incidence and mortality rates differ substantially across different regions in Africa. East Africa and West Africa have a high incidence and mortality rates as compared to North Africa. For example, Southern Africa has high confirmed cases of cervical cancer at a rate of 50 cases per every 100,000 people (GLOBOCAN, 2008).

In Kenya, cervical cancer is the second commonest cancer among women with the highest mortality rate (National guidelines for Cancer Management Kenya, 2013).The annual reported cases of cervical cancer are 2454 with 1676 deaths. By the year 2025, it's projected that the number of new cervical cancer incidences will peak at 4261 (Kenya National Cancer Prevention Programme-Strategic Plan, 2012-2015).

Management of cervical cancer employs the use of surgery, radiotherapy and chemotherapy or chemoradiotherapy. The modality chosen either for curative or palliative purposes is primarily dependent on the FIGO stage and patients' comorbidities (WHO, 2014).The initial therapeutic modality is mainly utilised for curative purposes. In addition, adjuvant chemoradiotherapy can be used to achieve tumour control or cure. Secondary therapy refers to palliative treatment aimed at improving the quality of life of the patient (WHO, 2013).

2.1.1 STAGE OF CANCER OF THE CERVIX

Cervical cancer staging is done to ascertain the extent of local disease and haematological and lymphatic spread to other organs. Staging is also valuable in the determination of how to manage the disease.

The cervical cancer staging is guided by the International Federation of Gynecology and Obstetrics (FIGO) recommendations .The FIGO staging does not take into account results of computerized tomography (CT), magnetic resonance imaging (MRI) or positron emission tomography (PET)(Porter *et al*., 2011).

Table 1: **FIGO Staging and Classification for Cervical Cancer**

FIGO STAGE	DESCRIPTION
I	Cervical carcinoma limited to the uterus.
IA	Invasive carcinoma seen at microscopic level.
IA1	Stromal invasion of the cancer.
IA2	Stromal invasion at a greater extent.
IB	The lesion is seen on clinical examination.
IB1	The lesion is visible on clinical examination and it has a dimension of not more than 4.0 cm.
IB2	The lesion is visible on clinical examination with the greatest dimension being 4.0 cm and above.
II	The primary lesion invasion is limited to the uterus and vagina.
IIA	There is no parametrial invasion.
IIB	Parametrial spread is evident.
III	The cancer spreads anteriorly invades the distal vaginal vault causing obstruction of the ureters with resultant hydronephrosis or renal failure.
IIIA	Cancer invades the distal vaginal vault but remains within the confines of the vaginal wall.
IIIB	The cancer spreads anteriorly causing hydronephrosis or renal failure.

IVA	Tumour spread extents to the anteriorly to the bladder or posteriorly to the rectal wall.
IVB	Presence of metastatic lesions.

Source: Management of Cervical Cancer. Scottish Intercollegiate Guidelines Network ISBN .www.sign.ac.uk, 2008.

The most important factors influencing prognosis are: stage of cancer; lymphadenopathy; tumour dimensions, extent of cervical spread and histology (Ericka *et al*., 2012). The FIGO recommendations state that the survival rate is good in stage one of the disease with a survival rate of 99.8%, 99.5%, 98.7% in 1, 2 and 5 years respectively. However, the good prognosis declines with the later stages of the disease to 45.8%, 23.9% and 15% in 1, 2 and 5 years (Ericka *et al*., 2012).

Puts *et al* (2013) in their study, it was revealed that factors associated with greater adherence were early stage disease with no metastatic spread. In addition, condition-related factors like the number of hospitalizations, presence of lymphadenopathy and cancer reoccurrence also lead to greater non-adherence (Puts *et al*, 2013).

2.1.2 TREATMENT RELATED FACTORS

Radiotherapy is the mainstay modality for treating patients with stage one and stage two diseases. It comprises of external beam radiotherapy (EBRT) and intracavitary brachytherapy (ICBT). Both EBRT and ICBT can be used in combination with chemotherapy. Radiotherapy involves making a trade-off between maximising the dose on the cancerous lesion (target) and minimising the dose on the adjacent normal tissues.

2.1.2.1 EXTERNAL BEAM RADIOTHERAPY

External beam radiation is applied through the use of linear accelerators. Intense photon energy beams of (> 10 MV) are projected to the target volume (tumour) which receives the highest dose with a minimal dose to the adjacent structures (Hellebust et al., 2009).Quadruple field technique

is employed in order to produce a maximum dose on the tumour volume and minimal dose to the adjacent tissues (Hellebust *et al*., 2009).

It is common practice to give relatively high energy photon radiation of (15–25 MV) since it spares the superficial tissues from unnecessary radiation. The use of quadruple field technique is employed to minimize the dose on the adjacent normal tissues in hospitals which have low energy Cobalt systems. The treatment technique is customized according to the tumor dimensions in order to achieve total disease control or palliation goal. In the recent times, simulation planning is being done through CT or MRI imaging to accurately delineate the target volume (Jhingran, 2008).

2.1.2.2 INTRACAVITARY BRACHYTHERAPY

Intracavitary brachytherapy is a radiotherapy modality which involves the application of one or more radiation emitting applicators in close proximity to the treated volume. The use of brachytherapy for curative or palliation of cancer of the cervix has been in use for over a century. In the inception days, the sources of radiation were from radium 226(Serkies *et al.,* 2001).

Modern brachytherapy has evolved from using radium sources of radiation. Currently, the use of low and medium dose brachytherapy is common. The radiation sources are mainly from caesium-137 and Iridium-192 radioisotopes (Hellebust, 2009). The mode of delivering brachytherapy treatment involves inserting hollow tubes (applicators) which emit radiation to the targeted cancerous tissue volume in the cervix. This method optimises the radiation dose emitted such that the tumour volume receives the maximum dose of radiation. There is inhomogeneity of the dose around the applicators and the dose emitted inversely proportional to the distance from the source (Hellebust, 2009).

Brachytherapy gives a curative effect similar to surgery (hysterectomy) during stages one and two of cervical cancer. In addition, it is the modality of choice for the late stages of the disease. Combining brachytherapy with EBRT and chemotherapy gives a superior therapeutic effect as opposed to when it is used alone (http://www.cancer.gov.).

Despite the beneficial effects of radiotherapy, adherence to treatment is vital. Poor adherence has often been associated with increased proliferation of cancerous cells and uncontrolled tumour spread. Hence, Adherence to the recommended radiotherapy treatment session's radiation prevents local and regional spread of the disease (Sabate, 2003). This ultimately increases survival and resultant remission of the disease. It also makes adherence crucial since radiotherapy plays an important role in the curative and palliative therapy of cervical cancer (William et al, 2007).

Treatment related factors affecting compliance to recommended radiotherapy can be due to patient or system related factors. Patient related factors include: interruptions to scheduled radiotherapy sessions due to frailties of patient; cultural or religious beliefs; inaccessibility to treatment centers and high cost of radiotherapy sessions. Systemic factors affecting adherence include: lack of proper coordination; deficiency in mobilization of resources; poor service delivery; increased number of patients and poor staging of cancer (Lebeau *et al.*, 2011).

Occurrence of therapy related side effects has been identified as one of the factors affecting adherence. Untoward effects of therapy have an influence on adherence rates despite the comorbidities the patient could having (Abdul *et al*., 2014) .A study in Switzerland in which it sampled a total of 177 cancer patients revealed that patients who had high adherence rates had less side effects (Winterhalder *et al.,* 2011). However, another study conducted by Bhattacharya and colleagues concluded that the development of side effects didn't have an effect on adherence (Bhattacharya *et al*., 2012).

2.1.3 SOCIO-DEMOGRAPHIC FACTORS

Socio-demographic factors refer to a set of variables such as age, marital status, level of education that affect adherence to radiotherapy treatment for patients with cervical cancer.

2.1.3.1 AGE

The older people are more susceptible to getting cancer than the younger generation. Older persons have more comorbidities than young people which in turn may have an effect on adherence to the treatment regime. Studies show that persons aged 75 years and above poorly adhere to the recommended treatment (Puts *et al*., 2013).Another study demonstrated that being

young in age, single with no comorbidities had a positive effect on adherence to treatment regimes (Kimmick *et al*., 2009).

In Kenya, women of the age of 15 years and above who are at higher risk of cervical cancer are estimated to be about 10.32 million. According to GLOBOCAN (2008), Kenya had 2354 cases of cancer of the cervix with 1676 cases of mortality reported annually. Cervical cancer is ranked as the second commonest form of malignancy afflicting women between the age of 15 and 44 years (Parkin *et al*., 2008). This age bracket also coincides with the reproductive age bracket. However, to my knowledge, there are no studies that have determined the relationship between age and adherence to radiotherapy treatment for cervical cancer in Kenya.

The graph shown on figure 3 is extracted from IARC report (GLOBOCAN, 2008) shows estimated age-specific incidence rates for cervical cancer in Kenya in comparison with estimates in Eastern Africa and the world.

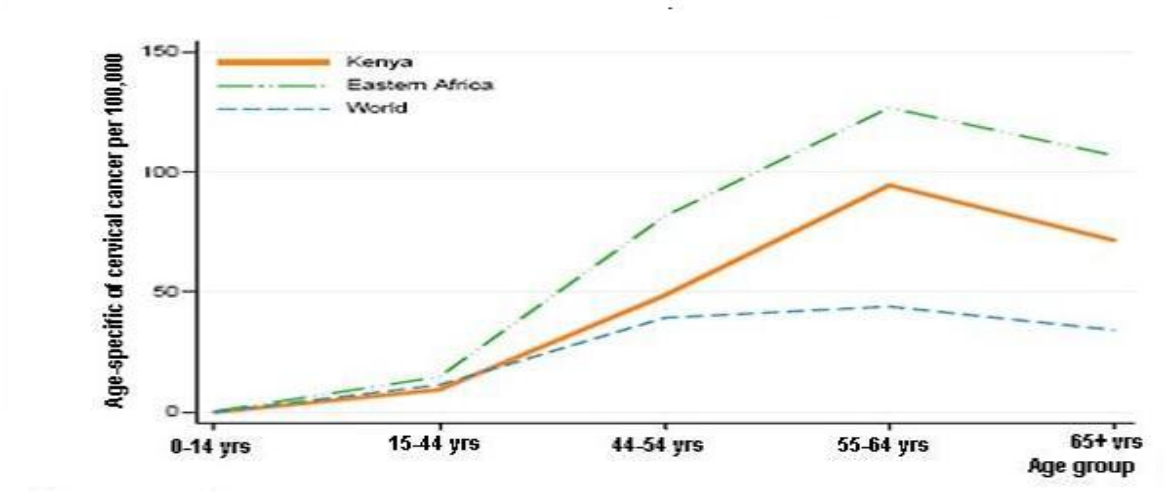


Figure 3: **Comparison between the incidence rates of cancer of the cervix and age.**
Source: GLOBACAN 2008

2.1.3.2 MARITAL STATUS

The marital status of a patient may have a positive or negative impact on adherence to the recommended treatment regime. Studies show that married persons are more likely to adhere to treatment regimens than unmarried persons due to spousal help in case of the former (Vlasnik *et al.,* 2005). According to another study, 106(48.04%) patients who were married were more compliant to treatment than unmarried patients 39(17.8%) (Gebre *et al*., 2012). However, this is contrary to other studies that show that marital status might influence patients' compliance with medication negatively**.**

2.1.3.3 LEVEL OF EDUCATION

Patients who have achieved a higher level of education may show have greater adherence rates. A recent study indicates that patients who had received formal education 191(60.8%) were more likely to be compliant as compared to illiterate patients 123(39.1%). Several studies have also lent credence to the theory that patients with higher educational level were associated with high adherence rates (Gebre *et al*., 2012).

2.1.3.4 MODE OF FINANCING

It's estimated that 40 % of the healthcare expenditure was financed through out of pocket mode of payment. Out of pocket payment is regarded by the WHO as a catastrophic mode of financing health care costs. The dependence on this mode of payment creates impediments to the accessibility to health services and drives people to penury (WHO, 2013). In addition, out of pocket financing doesn't provide financial risk protection to the patients. This creates a situation where sickness leads to poverty.

Financial access as well as physical inaccessibility to facilities offering health care services remains a serious problem in Kenya. The average total health expenditure per Kenyan is USD 42.2 which is sufficient to buy a basic package of essential health services. Financing for health services through out of pocket (OOP) constituted to 25% of the total health expenditure, showing that many Kenyans cannot rely on equitable pre-paid financing mechanisms. Nearly 15% of Kenyans spent more than 40% of non-food expenditure on health care. Health care is thus a major source of financial distress for many Kenyans (Muiya, 2013).

Out-of-pocket payments still form the greatest contributor to healthcare funding in Kenya (Chuma & Okungu, 2011). This is in contrast to developed countries which depend entirely on either taxes or mandatory national health insurance deductions. Least developed countries depend almost entirely on out-of-pocket financing than the other modes of payments.

Health insurance schemes in Kenya are the national health insurance fund (NHIF), private insurance and community-based health insurance fund (CBHIF). Private health insurance is mainly utilized by the middle and higher income citizens (Kimani *et al*., 2004).Community-based health insurance has a low penetration in Kenya, having been introduced in the year 1999. Data from the Kenya Community Based Health Financing Association (KCBHFA) indicate that there are 38 CBHI schemes, with a combined total of 100,510 active members (Kimani *et al*, 2012). Therefore, majority of Kenyans particularly those without insurance are not able to afford radiotherapy services. Such patients are likely to default on treatment sessions due to inadequate funds.

The National Health Insurance Fund (NHIF) created by an Act of Parliament Kenya is the only public health insurance scheme in the country. At inception, the intent of NHIF was to provide medical insurance cover for both privately and publicly employed persons whose gross minimum salary was Ksh 1,000 and above (Deolitte, 2011). The NHIF act has been amended severally to provide more benefits to other members especially those not employed by the government or private institutions and to extent the cover to both outpatient and inpatient medical services. In 1998, the NHIF act of 1966 was expunged from the constitution and substituted by the more comprehensive NHIF Act No. 9 of 1998 (Deolitte, 2011). This transformed the fund into an independent entity mandated to provide insurance to the Kenya population (Kamau & Holst, 2008).

The minorities of Kenyans with NHIF cover are employed in the formal sector and are mainly the middle and high income earners. Hence, the majority of low income earners are left without financial risk protection from ill health. Although NHIF allows voluntary membership for persons not employed in the formal sector, the number of such persons with medical cover is low (Chuma & Okungu, 2011). As aforementioned, Kenyan households are major contributors to

health expenditure. This widespread imposition of user charges presents an important barrier to utilizing services and has led many households into impoverishment where a chronic disease is involved.

Women in low income countries are less likely to adhere to treatment for breast and gynecologic malignancies which in turn contributes to the high cases of deaths (Kathleen *et al.,* 2009). Majority of the research studies have focused their attention to screening for cancer and patients follow up. In contrast, there is a paucity of studies done to empirically test interventions aimed at improving adherence to cancer treatment for patients with low incomes (Kathleen *et al*., 2009). Past research studies revealed that patients in least developed countries had poor adherence rates to radiotherapy in comparison to the national rates of (16% versus 63%), and this was attributed to interruptions to treatment at 64% and declining of treatment at 20% (Schleinitz *et al*, 2006).

An extensive study done by the Surveillance Epidemiology and End Results **(**SEER) which collected data from 24,510 patients, showed that patients who had insurance coverage had high rates of adherence at 87%.This was particularly for patients who received 25 or more sessions of radiotherapy (Kathleen *et al.,* 2009).This study provided the evidentiary proof that having a health insurance cover would result to better adherence to treatment.

Another study analyzed 3,193 patients diagnosed with colorectal cancer and it also demonstrated that 78.2% of the patients with insurance covers finished the recommended dose of chemotherapy. The two studies showed that there was a positive effect of treatment insurance to adherence to treatment (Ell *et al*, 2009).

There are no research studies done locally on the influence of health insurance to adherence to radiotherapy treatment. However, other comparable studies done on the effect of insurance on adherence to the prescribed chemotherapy sessions have shown that most of the patients with insurance covers had high adherence rates. Hence, based on these studies, insurance coverage is a significant factor affecting adherence to treatment.

2.2 RESEARCH QUESTION

What factors affect adherence to radiotherapy treatment for patients with cervical cancer?

2.3 HYPOTHESIS

I. Socio-demographic factors affect adherence to radiotherapy treatment for cervical cancer patients.

II. The stage of the disease has an effect on adherence to radiotherapy treatment for patients diagnosed with cancer of the cervix.

III. The mode of financing has an effect on the adherence to radiotherapy treatment for cervical cancer patients.

2.4 OBJECTIVES

2.4.1 BROAD OBJECTIVE

To determine factors affecting adherence to radiotherapy treatment for patients with cervical cancer.

2.4.2 SPECIFIC OBJECTIVES

The specific objectives are:

I. To identify the socio-demographic factors that affect adherence to radiotherapy treatment;

II. To determine whether the stage of the disease affects adherence to radiotherapy treatment;

III. To determine whether the mode of financing has an effect on adherence to radiotherapy treatment;

IV. To assess relationship between treatment time and adherence to radiotherapy treatment;

V. To determine whether the side effects of radiation therapy have an effect on adherence rates.

2.5 STUDY LIMITATIONS

The study area being a private institution, the factors affecting adherence to treatment may differ from those in public institutions. In addition, generalizability of the study findings to other setting especially public institutions may be difficult. It was also difficult to determine system related factors such as machine breakdowns or lack of qualified personnel which may have affected patients' adherence to treatment. Such information was not recorded in the electronic health records of the patients. In addition, these being a quantitative study, in depth information on patients' psychological factors or other comorbities that may affect adherence to treatment were not sought.

CHAPTER THREE: STUDY DESIGN AND METHODOLOGY

3.1 STUDY AREA

MP Shah Hospital was established in the 1930s to provide healthcare services to the communities living around Parklands. At the inception the hospital was referred to as the Parklands Nursing Home. Through the years, the vision of the hospital changed from provision of basic healthcare services to be a one stop healthcare facility for all Kenyans and persons living outside our borders (www.mpshahhosp.org).

MP Shah Cancer care center consists of the radiotherapy and chemotherapy departments. It was founded in 2010 becoming the first cancer care centre in the whole of Eastern Africa. It is fully equipped with the latest healthcare technologies to provide quality services to its clients (www.mpshahhosp.org). In addition, it has well trained and qualified human resource which provides highly specialized diagnostic and therapeutic services (www.mpshahhosp.org).

In the radiotherapy department, there are two linear accelerators equipped with micro multileaf collimator technology. This technology reduces radiation errors by accurate delivery of the radiation doses to the target tissue. The system allows highly trained radiotherapists to accurately deliver the photon beam energy to the target tissue with pinpoint accuracy (www.cancercarekenya.com).

Due to retrospective study design, the MP Shah cancer center was a favorable institution for data collection since it has a more comprehensive electronic database for its patients.

3.2 STUDY DESIGN

This was a quantitative retrospective descriptive study which gathered data from case files of women with histologically proven cancer of cervix who were treated at MP Shah cancer centre from 1st January 2012 to 31st December 2014.The study employed the use of the electronic database in which patients were randomly selected from the sampling frame according to the exclusion and inclusion criteria.

The researcher chose a retrospective study design because it employs the use of non-obstructive techniques of data collection and reduces the risk of Hawthorne effect. Studies show that if

patients are aware that they are being observed or monitored, it may have an influence in their compliance. This is due to the fact that patients who are aware that they are being observed may demonstrate a different behavior. The influence of the observation on the outcome of interest is termed the "Hawthorne effect" (Kathryn et al., 2009). Hence, the retrospective study avoided the bias that might have been introduced by the Hawthorne effect since the data was not collected directly from the patients but from the electronic database.

3.3 STUDY POPULATON

All patients with cancer of the cervix who were treated using radiotherapy between January 2012 and December 2014 with pelvic radiotherapy planned as part of standard treatment at the cancer center at MP Shah Hospital.

3.4 INCLUSION CRITERIA

I. All female patients diagnosed with biopsy proven cervical carcinoma.
II. Staging based on the FIGO recommendations.

3.5 EXCLUSION CRITERIA

I. Female patients having double primary cancers.

3.6 SAMPLE SIZE DETERMINATION AND FORMULA

The sample size will be determined using the epidemiological formula shown below (Wayne, 1999).

$$\mathbf{n} = \frac{Z^2 * (p) * (1-p)}{c^2}$$

Where:

Z = Z value (e.g. 1.96 for 95% confidence level)

p = prevalence of characteristic being estimated (in this case, prevalence of cervical cancer, 20%) (Kenya National Cervical Cancer Prevention Program: Strategic Plan 2012-2015)

c= confidence interval, expressed as decimal.

$$\mathbf{n} = \frac{(1.96)^2(0.2) * (1-0.2)}{}$$

$(0.05)^2$

n=246

3.7 SAMPLING METHOD

The sampling frame consisted of a list of all cervical cancer patients who underwent radiotherapy between January 2012 and December 2014 according to the inclusion and exclusion criteria. Probabilistic random sampling was used to draw 246 patients using a table of random numbers.

3.8 VARIABLES

3.8.1 INDEPENDENT VARIABLES

The following were the independent variables for the study.

i. Age of the patient
ii. Level of education
iii. Marital status
iv. Stage of cancer
v. Mode of financing
vi. Treatment duration
vii. Side effects of treatment

3.8.2 DEPENDENT VARIABLE

The dependent variable for this study was adherence to recommended radiotherapy treatment.

3.9 DATA COLLECTION INSTRUMENT

A close ended questionnaire (Appendix B) was used to record the relevant information from the electronic database .The closed ended questionnaire was structured to record the following information according to the specific objectives of the study:

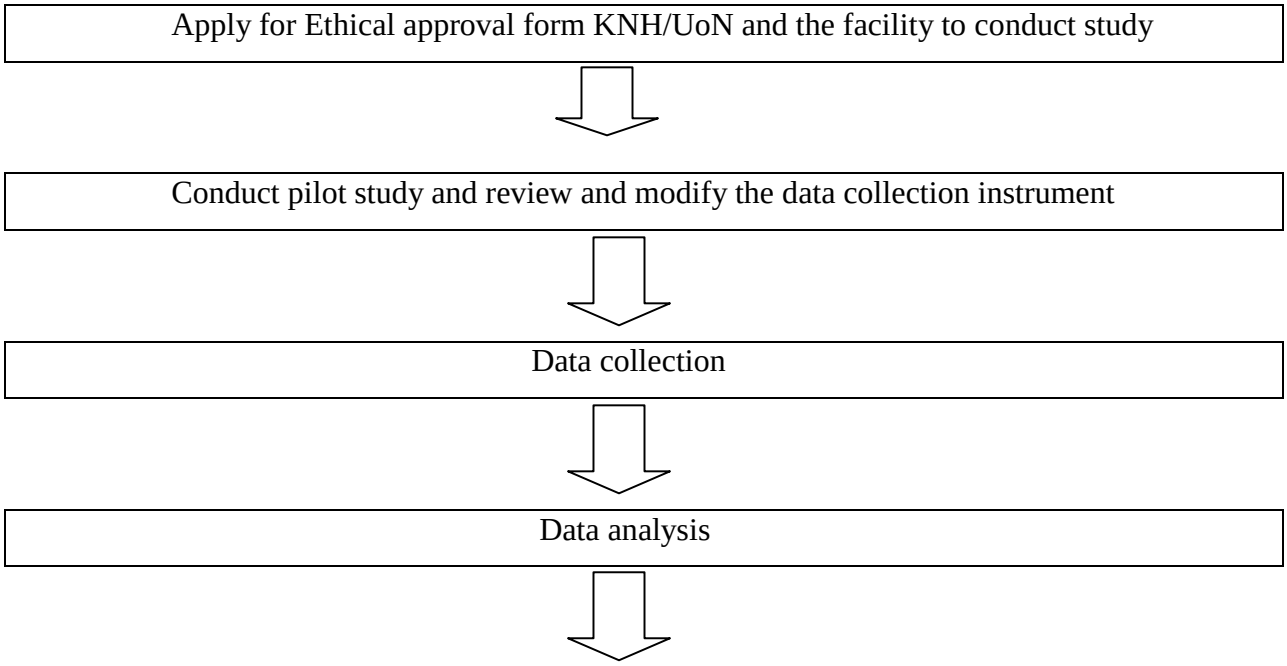
i. Socio-demographics factors
ii. Stage of cancer of the cervix
iii. Mode of financing
iv. Treatment time
v. Side effects of radiotherapy

3.10 DATA COLLECTION PROCEDURE

All cases of women with histologically proven cancer of cervix who were treated at MP Shah Cancer centre from 1st January 2012 to 31st December 2014 were reviewed. The study employed the use of the electronic database in which patients were randomly selected from the sampling frame according to the exclusion and inclusion criteria. The data was collected between 1st June and 20th June 2016.

The search term 'cervical cancer' and the period of interest (1st January 2012 to 31st December 2014) was entered into the electronic database to obtain the sampling frame. Probabilistic sampling was used to draw a sample of 246 patients using a table of random numbers according to the exclusion and inclusion criteria.

A closed ended questionnaire was then used (Appendix B) to capture the relevant information with regards to the study. Information regarding the patient's socio-demographic factors, stage of disease and mode of financing and compliance to treatment was retrieved from the electronic health records. In addition, the electronic health records provided data on the number of radiotherapy fractions, treatment time and the side effects of treatment on each of the patients randomly selected to form the sample.



Dissemination of Research findings

Figure 4: **Methodology of data collection**

3.11 DATA PROCESSING AND STATISTICAL ANALYSIS

The data was entered into the Epi info version 3.1 software and analysis done using statistical package for the social science (SPSS) version 20. Thereafter, the results were presented in form of tables, bar graphs, line graphs and pie charts.

Multivariate logistic regression analysis was used to show the association between the adherence to treatment (dependent variable) and the socio-demographic factors, mode of financing, and stage of disease, treatment time and side effects of radiotherapy among cervical cancer patients (independent variables).

3.12 CONFOUNDING FACTOR: DOUBLE PRIMARY CANCER

This refers to the presence of two or more primary cancers in a person. They are divided into synchronous (occurring at the same time) and metachronous (occurring at different times) (Howe, 2002).

The double primary tumours have different tumour characteristics which make the distinct from other types of malignancies (Howe, 2002). The staging and subsequent treatment of patients with double primary tumours differs from patients with a solitary primary tumour. Hence, patients with double primary tumours could be a source of confounding since the staging and treatment of the same is different from patients with a single primary tumour (cervical cancer).

3.13 PILOTING OF THE DATA COLLECTION INSTRUMENT

A pilot study was done to test the closed ended questionnaire (Appendix B). The questionnaire was piloted to determine its consistency and accuracy. A convenience sample of 20 medical records was used for the pilot study. Thereafter, the questionnaire was then restructured and modified to enhance its consistency and accuracy during data collection. The pilot study enabled the researcher identify any potential problems that could occur during data collection for the main study.

3.14 ETHICAL CONSIDERATIONS

Permission to conduct the research was granted by the Kenyatta National Hospital and University of Nairobi (KNH/UoN) ethics and research committee and the MP Shah Hospital ethics review board.

An informed consent was used to get permission for study participation from the patients. To ensure confidentiality and anonymity, names of patients' names were not used in the final dissertation or presentation of the study findings. The obtained information was used for the approved research purposes only. There were no direct or indirect untoward effects to the study participants included in the sample.

CHAPTER FOUR: RESULTS

This chapter gives a summary of the study results and discussion after statistical analysis of the collected data.

4.1 SOCIO-DEMOGRAPHIC FACTORS

This included age, marital status and level of education.

4.1.1 AGE

The mean age of the patients was 57 years. Of the 226 randomly selected patients: 9.3% were in the age stratum of 30-39 years; 24.3 % in age stratum of 40-49 years; 26.5 % in the age stratum of 50-59 years; 22.1% in the age stratum of 60-69 years; 11.9% in the age stratum of 70-79 years; 5.3 % in the age stratum of 80-89 years and 0.4 % in the age stratum of 90-99 years. Hence, the majority of patients were between the ages of 50-59 years (Figure 5).

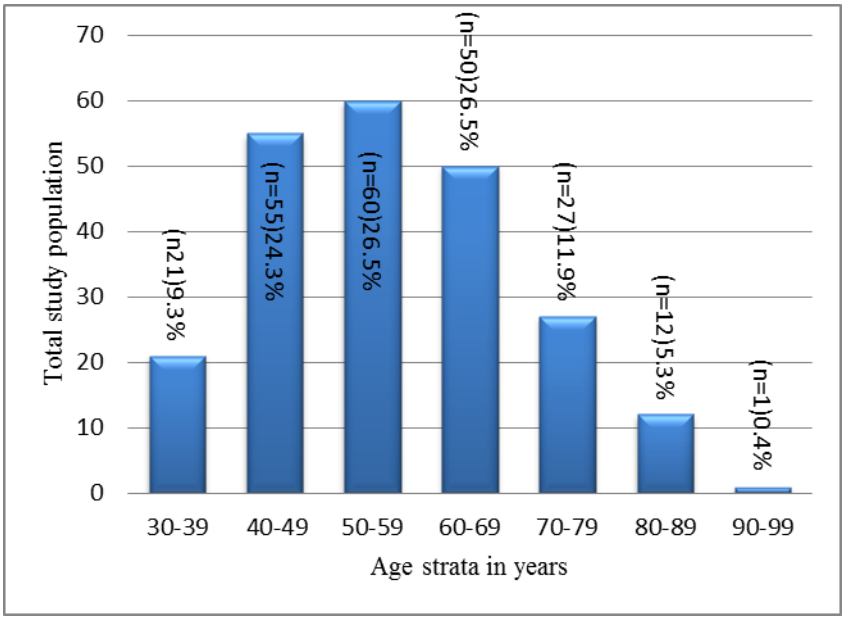


Figure 5: **Age strata for the study participants (n=226).**

4.1.2 MARITAL STATUS

Unmarried (single) patients constituted 25.7% (n=58) while married patients constituted 53.5% (n=121) of the sample population. Divorced and widowed patients constituted 7.5% (n=17) and

13.3 % (n=30) of the sample population respectively. Married patient's represented more than half of the patients sampled.

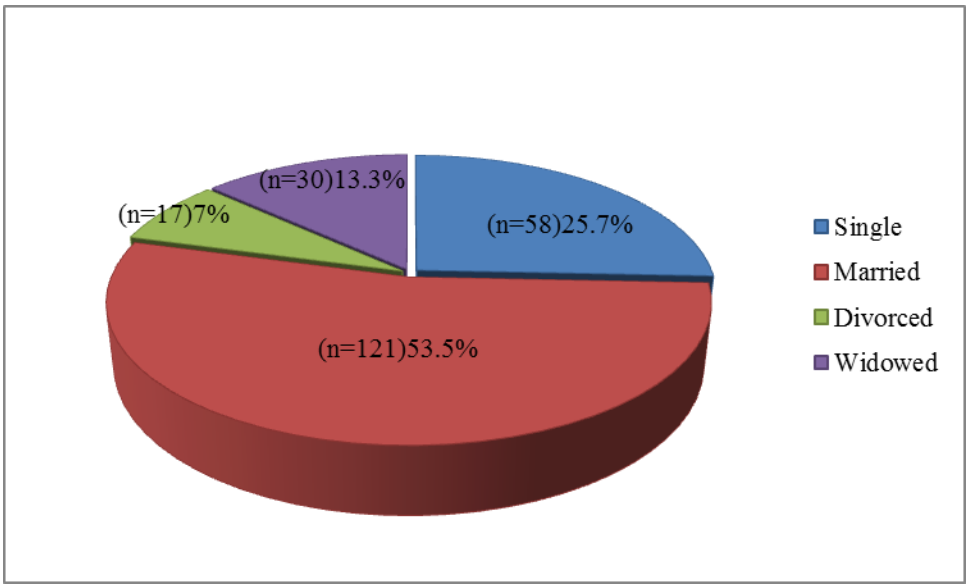


Figure 6: **Marital status of study participants (n=226).**

4.1.3 LEVEL OF EDUCATION

Thirty four (15.1%) patients had attained a primary level of schooling. Sixty nine (30.5%) patients had a secondary level of education while one hundred and twenty three (54%) patients had attained a tertiary level of schooling. Most of the patients in the study sample had a tertiary level of education (Figure 7).

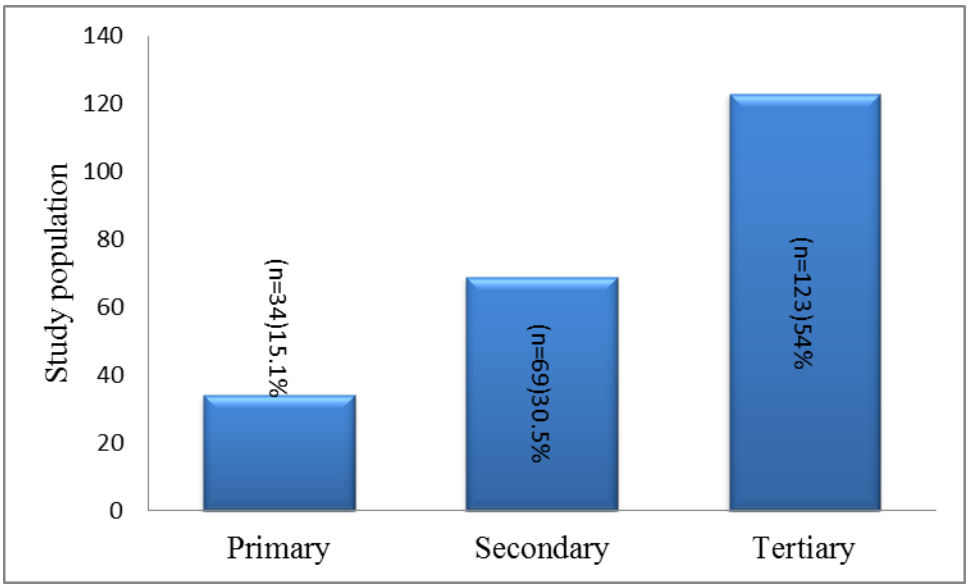


Figure 7: **Level of education of study participants (n=226).**

4.2 MODE OF FINANCING

One hundred and two (45.1%) patients paid for radiotherapy through private insurance. Eighty (35.4%) patients representing of the patients sampled for the study used the national health insurance fund cover to pay for the radiotherapy treatment. A total of forty four (19.5%) patients financed their radiotherapy treatment costs through out of pocket method. None of the patients in the sample used community based health insurance fund to pay for the radiotherapy services (Figure 8).

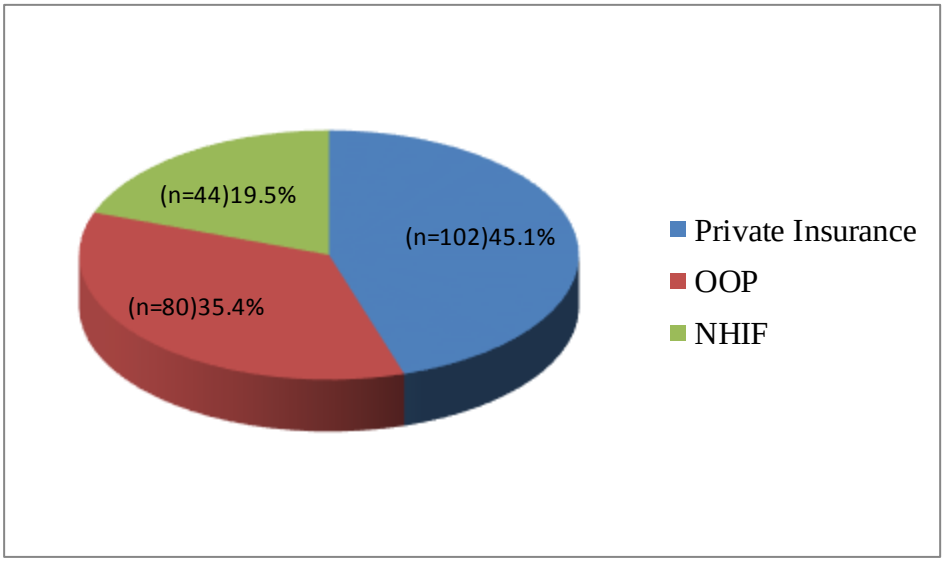


Figure 8: **Mode of financing (n=226).**

4.3 STAGE OF DISEASE

Forty two patients representing 18.6 % were diagnosed with stage one of cancer of the cervix. One hundred and one (44.7%) patients had stage two cancer of the cervix. Fifty seven patients representing 25.2 % (n=57) had stage three cancer while twenty six (11.5%) patients were diagnosed with stage four disease (Figure 9).

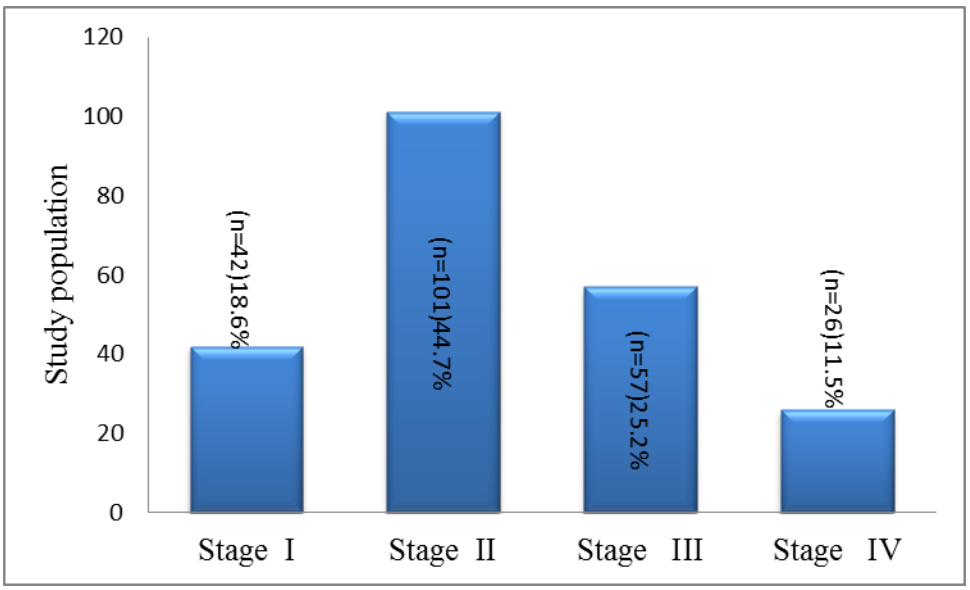


Figure 9: **FIGO stage of cervical cancer at diagnosis (n=226).**

4.3 SIDE EFFECTS

The commonly reported side effect of radiotherapy was cutaneous effects which affected two hundred and six patients representing 91.2% of the sample population. Neurological and urological side effects constituted 7.1 %(n=16) and 1.8% (n=4) respectively.

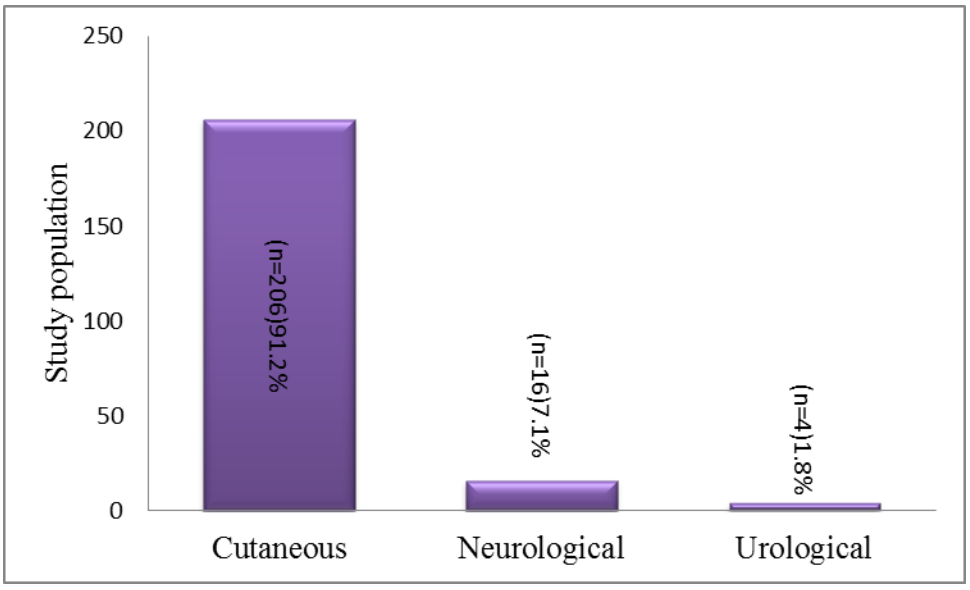


Figure 10: **Side effects of radiotherapy (n=226).**

4.4 INFERENTIAL STATISTICAL ANALYSIS.

Inferential statistics were used to show the association of the dependent variables to the independent variable. The dependent variable (adherence to the recommended radiotherapy treatment) was compared to the independent variables (age; level of education; marital status; mode of financing; treatment time and side effects to radiotherapy.

Table 2**: Inferential statistical analysis on the association between dependent variable and the independent variables.**

Population Characteristic				**Adherence to Treatment**		
Social Demographic						
Marital Status	**N**	**Totals**	**%**	**n**	**%**	**p-values**
Single	58	226	25.7	47	20.8	
Married	121	226	53.5	119	52.7	0.0001*
Divorced	17	226	7.5	10	4.4	
Widowed	30	226	13.3	14	6.2	
Total	226	226	100.0	190	84.1	
Mode of Financing						
OOP	44	226	19.469	15	6.63717	

Private Insurance	102	226	45.1327	100	44.2478	0.234
CBHIF	0	226	0	0	0	
NHIF	80	226	35.3982	64	28.3186	
Total	226	226	100	179	79.2035	
Stage of the Disease						
I	42	226	18.6	37	16.4	
II	101	226	44.7	94	41.6	0.002*
III	57	226	25.2	47	20.8	
IV	26	226	11.5	11	4.9	
Total	226	226	100.0	189	83.6	
Side Effects						
Cutaneous	206	226	91.2	115	50.9	
Neurological	16	226	7.1	3	1.3	0.034*
Urological	4	226	1.8	1	0.4	
Total	226	226	100.0	119	52.7	
Level of Education						
None	0	226	0	0	0	
Primary	34	226	15.0442	11	4.86726	
Secondary	69	226	30.531	45	19.9115	0.002*
Tertiary	123	226	54.4248	98	43.3628	
Total	226	226	100	154	68.1416	

Stage of the Disease					**Frequency**	**%**	**p-values**
	n	**Total**	%	**Treatment Time**	**N**		
I	42	226	18.6	25 DAYS	27	11.9	
II	101	226	44.7	28 DAYS	44	19.5	0.002*
III	57	226	25.2	28 DAYS	47	20.8	
IV	26	226	11.5	> 30 DAYS	11	4.9	
Total	226	226	100		129	57.1	
Age in Years							
20-29	0	226	0		0	0	
30-39	21	226	9.3		15	6.6	
40-49	55	226	24.3		50	22.1	0.007*
50-59	60	226	26.5		43	19	
60-69	50	226	22.1		32	14.2	
70-79	27	226	11.9		13	5.8	
80-89	12	226	5.3		4	1.8	
90-99	1	226	0.4		0	0	
Total	226	226	100		157	69.5	

**Significant at 0.05*

The stage of the disease showed association with the adherence of the treatment among the patient treated with ($\chi 2$=5.945; df= 3 p-0.015). However, adherence to treatment was very low at the late stages of the disease (Figure 11).

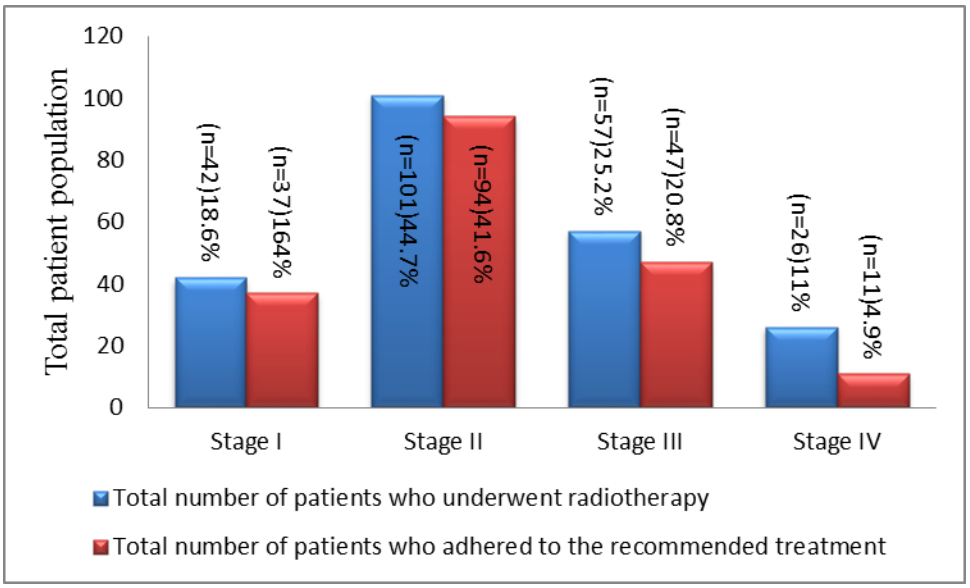


Figure 11: **The association between the stage of disease and the adherence rates (n=226).**

Marital status was significant factor in explaining adherence to treatment with ($\chi 2$=4.945; df= 3 p=0.001) at bi-variate level. It implies that there is association between compliance to treatment and the marital status. Most of the patients that showed high adherence were married 121/226(52.7%) despite that it had the highest number of patient administered for the treatment (Figure 12).

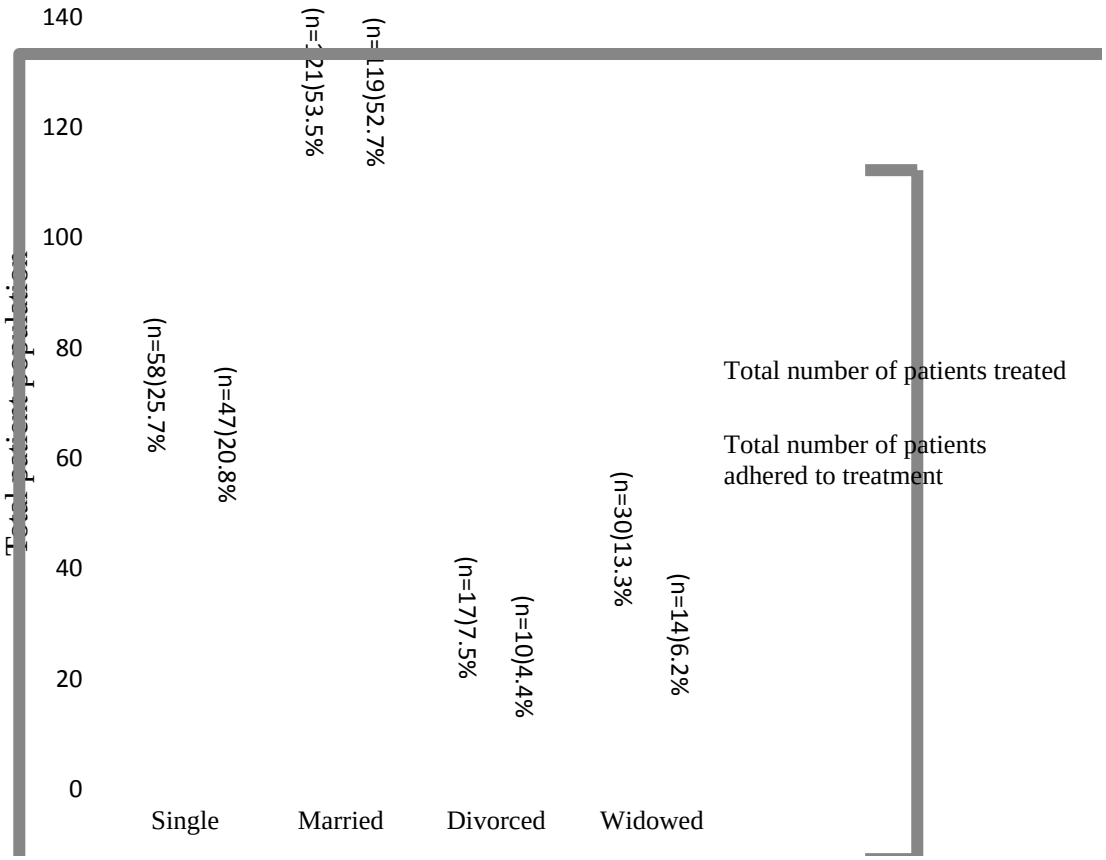


Figure 12: **Relationship between marital status and adherence to radiotherapy treatment (n=226).**

Bivariate analysis revealed significant relationship between the untoward effects of radiotherapy and the compliance to the treatment with ($\chi 2$=10.945; df= 2 p-0.034).Patient with cutaneous side effects were the majority at 91.2% with 50.9% adhering to treatment (Figure 13).

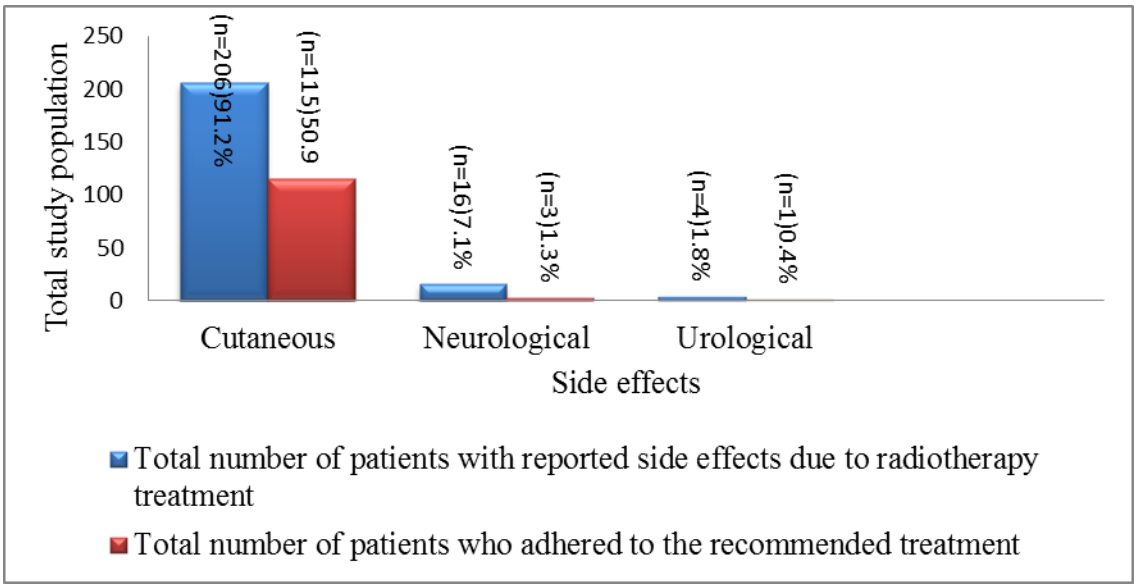


Figure 13: **The relationship between side effects and adherence to treatment (n=226).**

The level of education showed a positive relationship with compliance to treatment with (χ2=p.945; df= 3, p-0.002).Most of those who completely adhered to treatment had tertiary level of education (Figure 14).

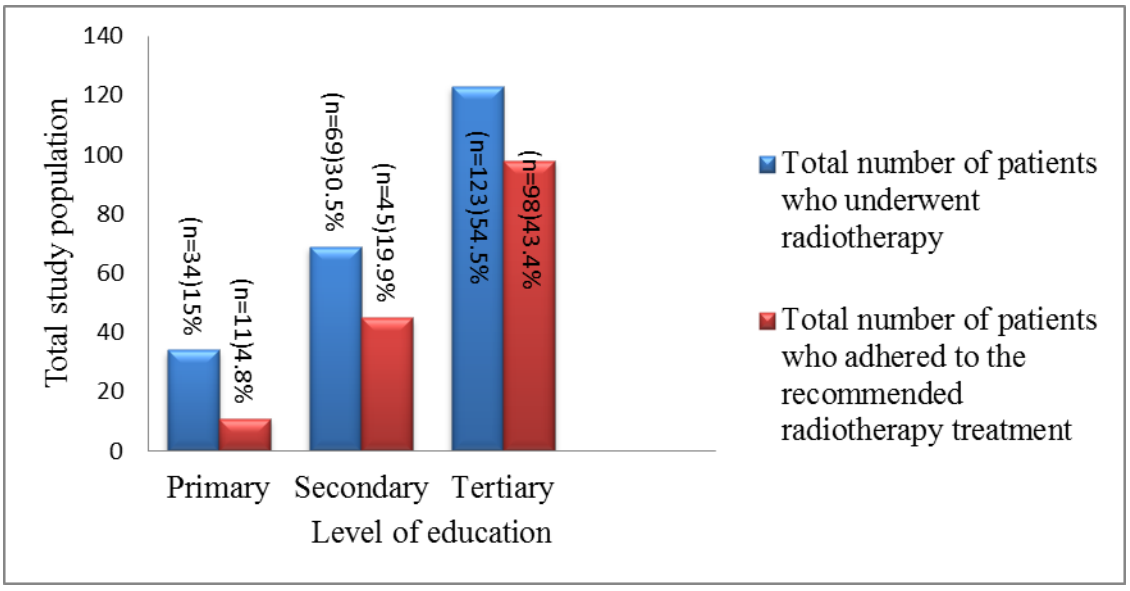


Figure 14: **The association between the level of education and adherence to treatment (n=226).**

Time of treatment adherence was found to have association with adherence to radiotherapy treatment depending on the stage of the cancer with (χ2=3.945; df= 3 p-0.0021).Many of those

who revealed adherence to treatment were in stage three with a time of treatment of 28 days(Figure 15).

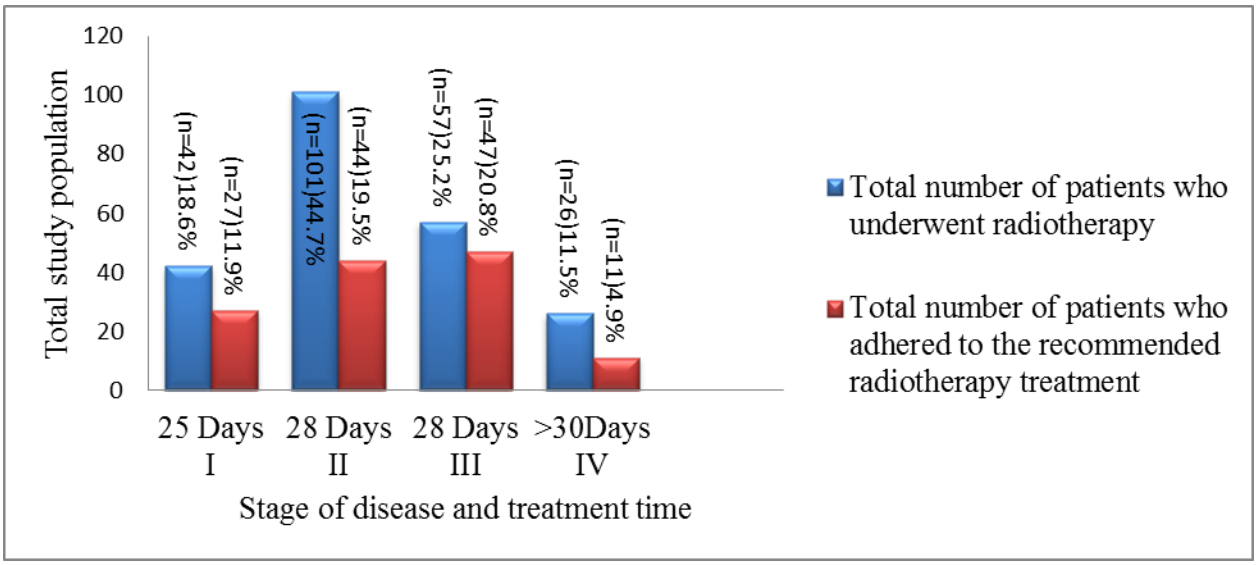


Figure 15: **Relationship between treatment duration, stage of disease and adherence to radiotherapy treatment (n=226).**

Age of the patient showed significant association with adherence to treatment with ($\chi 2$=1.945; df= 7 p-0.008).Many of the patients who showed adherence to treatment were between the ages 40-49 years (22.1%) (Figure 16).

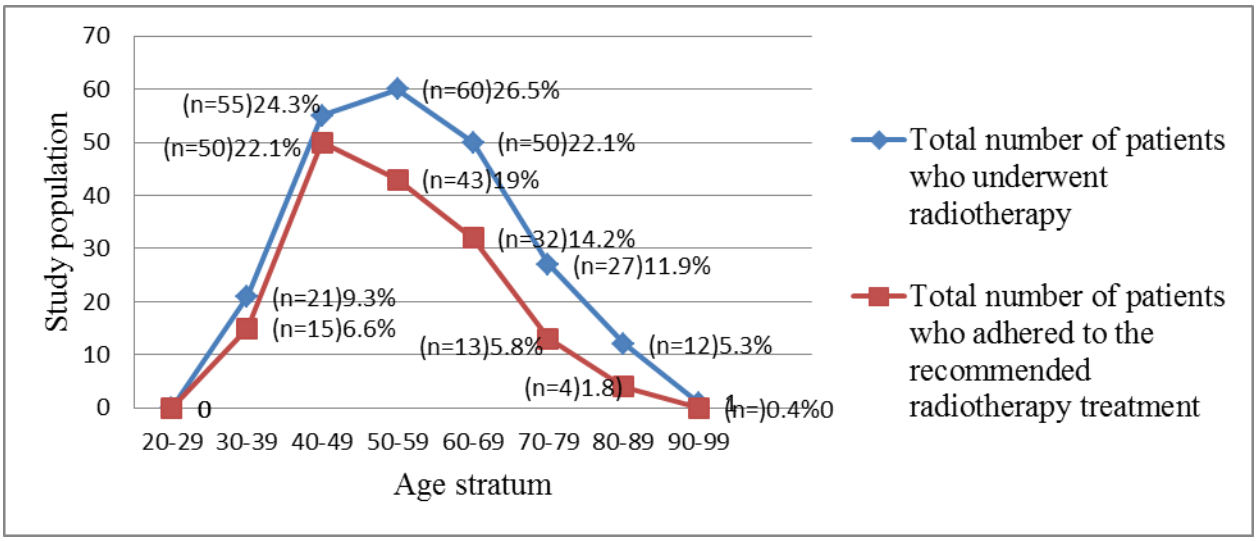


Figure 16: **The association between age and adherence to treatment(n=226).**

The mode of finacning did not show significant association to treatment with a p-value of 0.234.Patients who financed their radiotherapy sessions using private insurance had the highest adhrerence rate at 44.2%.Patients with private insuarance constituted to 45.1 % of the sample population.Simirilary,patientswho used NHIF as a mode of payment had the second highstes adherence rate with 28.3 % of the patients adhereing to treatment(Figure 17).

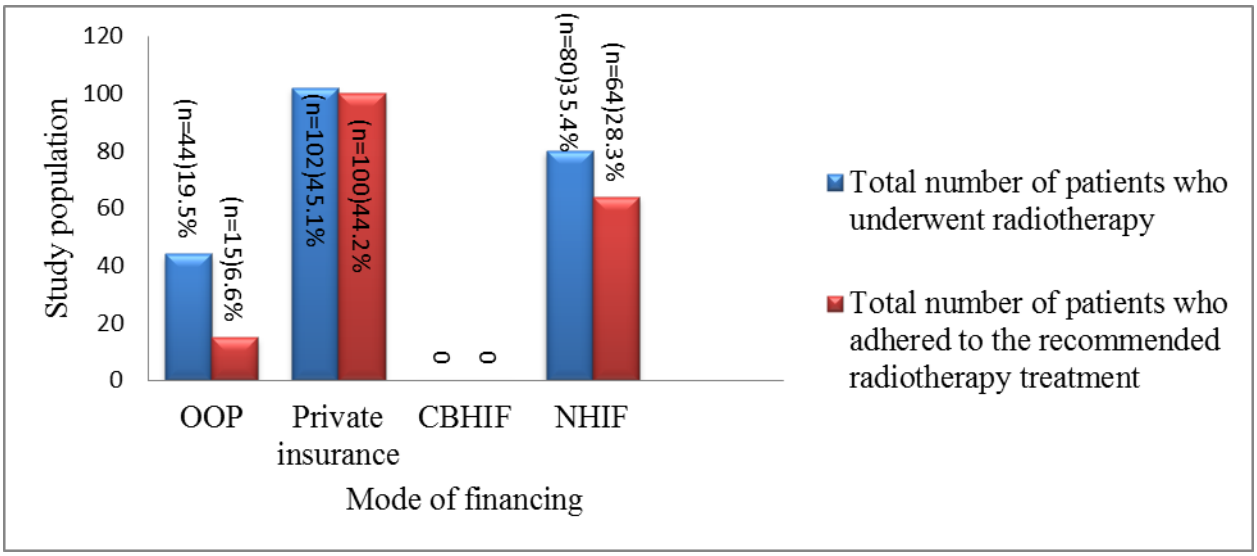


Figure 17: **The association between mode of financing and adherence to treatment (n=226).**

4.5 MULTIVARIATE ANALYSIS

Multiple binary logistic regressions were employed to investigate the effect of age, education level, stage of the disease, treatment time and side effects on the adherence to cervical cancer treatment.

Table 3: **Multivariate Analysis.**

Population Characteristics	Adjusted OR	P-values	CI for OR
Marital Status			
Single	**		
Married	0.2	<0.0001***	0.107-0.81
Divorced	1.21	<0.0021***	0.8-5.14
Widowed	0.31	<0.001***	0.12-0.967
Education Level			
None	**		
Primary education	0.512	<0.0001***	0.213-0.978
Secondary education	0.54	<0.0001***	0.234-0.80
Tertiary	1.54	<0.0001***	0.38-5.78

Stage of the Disease				
I	**			
II		0.93	0.00135***	0.387-5.12
III		0.56	0.00305***	0.230-3.97
IV		0.12	0.0001***	0.078-1.35
Mode of Financing				
CBHIF		**		
OPP		1.11	0.00315***	0.287-3.97
NHIF		1.3	<0.0001***	0.98-5.170
Private Insurance		1.5	<0.0001***	0.38-2.34
Side Effects				
Cutaneous	**			
Neurological		1.211	<0.0001***	0.144-6.696
Urological		0.058	<0.0001***	0.230-3.97
Treatment Time				
Stage I (25 days)		1.318	<0.0001***	0.234-7.80
Stage II (28 days)		1.07	<0.0001***	0.28-5.89
Stage III (28 days)		0.276	<0.0001***	0.234-0.80
Stage IV (> 30 days)		**		
Age of Patient				
20-29	**			
30-39				
40-49		1.878	<0.0011***	0.148-6.676
50-59		0.43	<0.0001***	0.153-3.98
60-69		0.11	<0.0001***	0.007-1.98
70-79		0.32	<0.0001***	0.023-0.965
80-89		0.105	<0.0001***	0.0111-0.876
90-99		0.085	<0.0001***	0.007-0.912

****Significant at 0.05 OR Odds Ratio** Reference Category CI-Confidence Interval*

Marital status showed negative association to the adherence of the treatment. Those who were divorced were 1.21 times more likely to not comply with the recommended treatment in comparison to those who were single (Table 3).

Those who used out of pocket to finance for their treatment were 1.11 times to adhere to treatment. Those who financed their treatment through NHIF were found to significantly adhere to treatment by 1.3 times more as compared to those who financed through out of pocket method. For private insurance as a mode of financing for radiotherapy treatment, the patients were 1.5 times more likely to comply with recommended therapy in comparison to those who used the other financing methods. The significance behind the financing mode is that if the financial resources are available and the treatment administered in the early stages, it would increase the chances of the patient adhering to treatment (Table 3).

Patients with tertiary level of education were found to adhere to treatment by 1.54 times more than those who had no education. This shows that education plays a vital role in disease management which in turn leads to a significant positive effect on adherence to treatment (Table 3).

Patients diagnosed with stage one; two and three of cervical cancer had a significant positive relationship to adherence. However, in the stages one and four of the disease revealed low chances of treatment adherence. Those patients with reported neurological and urological side effects were found to have a negative relation with adherence to treatment. Patients experiencing urological side effects were 0.058 times more likely to adhere to treatment as compared to those with cutaneous side effects (Table 3).

Treatment at the early stages (stage two) within 28 days showed a significant positive effect on the adherence to treatment. Those patients who were treated within 25 days revealed adherence to the treatment by 1.32 times more than those whose treatment commenced after 30 days (Table 3).

CHAPTER FIVE: DISCUSSION

The aim of this study is to determine factors affecting adherence of patients with cervical cancer to radiotherapy treatment. The specific objectives are: to determine whether socio-demographic factors; the stage of the disease; the mode of financing; the treatment time and the side effects of radiation therapy had an effect on adherence to radiotherapy treatment. The relevant data was obtained from a total of 226 subjects who were randomly selected from the sampling frame and who underwent radiotherapy between 1st January 2012 and 31st December 2014 at the M.P.Shah cancer center.

5.1 AGE

This study showed that age had a significant effect to adherence to the recommended radiotherapy treatment. Most of the patients were between the ages of 40-49 years (24.3%) and the ages of 50-59 years (26.5%).The two age groups formed approximately half of the total patients sampled with a combined percentage of 50.8%.These findings are in contrast to studies done locally within the Eastern Africa region.

The Kenyan study done by Innocent *et al* (2013) found out that the age of patients ranged between 21 years to 94 years with a mean of 49 years. The incidences of cancer of the cervix peaked at the age of 47 years. However, the average age of patients in this study was 57 years. This implies a shift of disease burden from the reproductive age to later stages of life.

This is also consistent with another study done by Samrat *et al* (2013) which revealed that middle aged women (40-50 years) with cervical cancer were more adherent to the recommended radiotherapy treatment. The contributory factor to the adherence was that these women did not have more than two children at home. The older people are more susceptible to getting cancer than the younger generation.

In this study, patients between the ages of 60 to 99 years of age had poor adherence rates. This was similar to a study done by Puts *et al* (2013) showed that persons aged 75 years and above poorly adhered to the recommended treatment. According to that study, older persons have more

comorbidities than young people which in turn may have an effect on adherence to the treatment regime (Puts *et al.,* 2013).

However, this study did not investigate the correlation between childbirth or the number of children to adherence to the recommended radiation therapy sessions. Currently, there are no local studies on the role of age on adherence to radiotherapy treatment for cervical cancer patients'.

5.2 LEVEL OF EDUCATION

The level of education had a significant positive effect on the adherence to treatment. Patients with tertiary level of education were found to adhere to treatment by 1.54 times more than those who had no education. This shows that education plays a key role in disease management which helps in adherence to the treatment.

The results of this study are similar to those of the International Journal of Cancer Studies and Research (IJRC) study done in 2012.It indicated that a higher percentage of the patients diagnosed with cancer of the cervix who had a high level of education were more adherent 191(60.8%) than those of participants who were illiterate 123(39.1%). The study also showed that educated patients were more adherent than illiterate patients.

5.3 SIDE EFFECTS

Majority of the patients representing had cutaneous side effects as a result of pelvic radiation. However, the cutaneous side effects didn't have a negative effect on adherence to treatment. Hence, the dermatological side effects are tolerable and they do not affect the adherence rates. Similar studies show that grade one and grade two skin reactions are common during treatment sessions, with 10% to 50% incidences rates being reported (Akila *et al.,* 2014).

Ngungi (2011) observed that radiation induced dermatological toxicity was the commonest reported side effect of pelvic radiotherapy. Radiation therapy toxicities to the skin had an effect on the patient's adherence. These untoward effects affecting the skin resulted in 36% (70; n=196) of the study participants either becoming non adherent to the recommended therapy (Ngungi, 2011).This is contrast with this study results.

A study in Switzerland in which it sampled a total of 177 cancer patients revealed that patients who had high adherence rates had fewer side effects (Winterhalder *et al.,* 2011). However, another study conducted by Bhattacharya and colleagues concluded that the development of side effects didn't have an effect on adherence (Bhattacharya *et al.,* 2012).

5.4 MODE OF FINANCE

The predominant mode of payment for radiotherapy sessions in this study was through insurance payments. These results are comparable with a local study done in public hospital by Ngondi (2011) that showed that 95.7% had NHIF insurance which was only used when one is admitted. Only 2.6% of the respondents in that study had private insurance .Currently there are no local studies on adherence to radiotherapy in private hospitals.

This study showed that having insurance was not a significant factor affecting adherence to treatment. An extensive study done by the Surveillance Epidemiology and End Results (SEER) which collected data from 24,510 patients, showed that patients who had insurance coverage had high rates of adherence at 87%.This was particularly for patients who received 25 or more sessions of radiotherapy (Kathleen *et al.,* 2009).This study showed having insurance was not a significant factor are more likely to adhere to radiotherapy treatment than those without (Ell *et al.*, 2009).

5.5 STAGE OF DISEASE

The peak incidence of cervical cancer in this study is comparable to similar studies conducted in developing countries.In a study by Gebre *et al* (2015), all cervical cancer patients included in the study (n=132), 42.0% were diagnosed at FIGO stage three while 99 (31.5%) had FIGO stage two. Locally, a study by Innocent *et al* (2013) revealed that most of the study participants 136/355(38.3%) presented with stage two disease and 148/355 had stage three disease which represented 80.5 %.

Another study done by Sahil *et al* (2016), the incidence peak age of the disease was 49 years with the histological analysis of tissue sample proving that squamous cell carcinoma was the commonest histological kind. All the study participants had FIGO staging to determine the extent

of the disease. Stages I, II, III and IV were found in 9.5%, 48.8%, 39.3% and 1.7% of the cases respectively.

The stage two of cervical was a significant factor affecting adherence to the prescribed treatment by patients. However, adherence to treatment was very low at the late stages of the disease. In the late stages of disease (stage four) revealed low chances of treatment adherence. In the early stages the adherence to treatment was found to yield significant positive effect. There is a paucity studies done on the effect of stage of disease to adherence rates.

5.6 MARITAL STATUS

In this study, patients who were married had a significant positive effect on adherence in comparison to unmarried, divorced and widowed patients. These results are relatively similar to studies done by Majinge (2011) and Ngondi *et al* (2011).

In the study done by Majinge(2011) on treatment outcomes of cervical cancer patients, the married patients were 411 (65.2%) were more adherent than single 17 (2.7%); divorced/separated 51 (8.1%);widowed 147 (23.3%).Similarly, Ngondi *et al* (2011) observed that 50.4% were married and had a high adherence rate than widowed, divorced and single patients.

In this study, marital status was significant factor in explaining adherence to treatment with chi square ($\chi 2=4.945$; df= 3 p=0.001) at bivariate level. It implies that there is a negative association between adherence to treatment and marital status. Majority of the patients that showed high adherence were married 121/226(52.7%).Those who were divorced had a likelihood of 1.21 times of adhering to recommended radiotherapy sessions in comparison to those who were single.

5.7 TREATMENT TIME

The standard radiotherapy treatment time for patients with stage one disease was 25 days while those with stage two disease had 28 days of treatment. Patients diagnosed with stage three and four received radiotherapy fractionated dose for a period of 28 days and more than 30 days respectively.

A similar study showed only 28 (50%) patients received optimal radiation therapy, with the majority (24/28) of them completing radiation therapy in 8 weeks (range: 6–8 weeks). The patients who were not able to get optimal radiotherapy, the median number of weeks to completing radiation therapy was 11 weeks (range: 4–24 weeks; 1 patient stopped treatment after 4 weeks) (Juan *et al.*, 2014).

In this study, the duration of treatment was found to have a correlation with adherence to radiotherapy treatment depending on the stage of the cancer with ($\chi 2=3.945$; df= 3 p-0.0021).Most of those who revealed adherence to treatment were in stage three with 28(20.8%).Patients who received treatment for more than 28 weeks showing low adherence levels.

In other comparative studies, non-adherence to pelvic radiation was associated with prolongation of treatment for over 56 days. The longer treatment duration contributed to poorer survival probability. However, radiation treatment delivered in less than 8 weeks improved local disease control and overall survival (Juan *et al*, 2014). Sahli *et al* (2016) in their study showed a direct relationship between long duration of radiotherapy and poor survival outcomes. This was comparable to a past study done by Juan *et al* (2014) in which the treatment duration of more than 56 days was found to have an effect on adherence, overall survival and local disease control (Sahli *et al*, 2016).

Majority of studies done on radiotherapy treatment duration concentrated on the role of treatment on survival rates and locoregional control of the disease. To the best knowledge of the researcher, none of the studies investigated the correlation of radiotherapy treatment duration and adherence rates in cervical cancer patients.

CHAPTER SIX: CONCLUSION AND RECOMENDATIONS

6.1 CONCLUSION

This was a retrospective quantitative study. The study population composed of all cervical cancer patients who underwent radiotherapy between January 2012 and January 2014 with pelvic radiotherapy planned as part of standard treatment at the cancer center at MP Shah Hospital. The researcher employed the use of the electronic database in which 226 patients were randomly selected from the sampling frame according to the exclusion and inclusion criteria. Out of these 40 patients were lost to follow up.

The aim of this study was to determine factors affecting adherence to radiotherapy treatment for patients with cervical cancer. The specific objectives were: to determine whether socio-demographic factors; the stage of the disease; the mode of financing; the treatment time and the side effects of radiation therapy have an effect on adherence to radiotherapy treatment.

Therefore, the study identified the following factors which have a significant positive effect on adherence to the recommended treatment. These are: being married ; having a tertiary level of education; being between the age stratum of 40-49 years; being diagnosed with stage two of cervical cancer; having a treatment duration of less than 28 days and having less side effects.

6.2 RECOMENDATIONS

The recommendations of this study can be summed up based on the WHO guideline which characterizes 'Adherence' as a multidimensional phenomenon composed of patient, disease/condition, therapy, health systems and social economic factors (WHO, 2014).

I. Patient related factors(Age and marital status):

Close monitoring of patients below the ages of 39 years and those above the age of 60 years in order to prevent treatment disruptions. Further research studies should done to ascertain the reasons why certain age groups show high adherence to radiotherapy than others.

II. Disease/condition related factors and Treatment/therapy related factors (Treatment duration, side effects of radiotherapy, FIGO stage of disease).

Dose optimization through careful simulation and dosimetric planning so that the primary tumor receives the maximum dose while the adjacent tissues minimal or negligible radiation dose. This measure will reduce the untoward effects associated with pelvic radiation thereby increasing the

adherence rates. In addition, closely monitoring patients with neurological and urological side effects of radiotherapy should be done to avoid this cohort of patients defaulting treatment.

Treatment duration should be standardized through development of standard treatment protocols to ensure that the treatment does not exceed 28 days for early stage disease. For patients advanced disease, treatment regime should be individualized to avoid intolerable side effects which may contribute to disruption of treatment sessions.

III. Health systems related factors (Electronic health records)

Establishment of electronic health records in all hospitals. This will provide an accurate, current and complete data on patients undergoing radiotherapy treatment. The electronic data will provide information on adherence of patients to treatment and the therapy related side effects which enables careful monitoring of patients who are likely to default treatment.

IV. Social economic factors (Literacy rate)

The government should widen the scope of national education to include the importance of adhering to treatment and the dangers of defaulting treatment through public programmes. In addition, there should be inclusion of adherence to treatment to the national cancer prevention and control programme.

Further research studies should done to ascertain the reasons why certain age groups show high adherence to radiotherapy than others.

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APPENDIX A:INFORMED CONSENT FORM

Source: Modified input from WHO (Informed consent form template for clinical studies).

Hello, my name is Martin Ian Kamanda. Am currently a second year student at the University of Nairobi doing a Master of Science degree in Health Systems Management. I am conducting a study on determinants of factors affecting adherence to radiotherapy treatment among patients with cervical cancer at the M P SHAH hospital. The objectives of this study is to determine whether sociodemographic factors, stage of disease, mode of financing, treatment duration and side effects of radiotherapy affect adherence to radiotherapy treatment for patients with cervical cancer.

You have been selected through random sampling to participate in this study. I am hereby inviting you to participate in this study. You will be assigned a specific code for identification. This will ensure your anonymity as regards tour participation in the study. Data collected will not be divulged to any other person apart from the research participants. When publishing the results of this your particulars will not be mentioned anywhere in the dissertation.

There are no direct benefits to you with regard to your participation in the study. However, the study recommendations may be vital for the program managers, stakeholders and researchers to recognize the status of cervical cancer survivors and co-morbidities and commence treatment and improve quality of life. This research will be used as a base line for policy makers, researchers and voluntary institutions since there is a little research conducted on cervical cancer in Kenya.

There will be no risk to you either directly or indirectly as a consequence of your participation in this study. The researcher will endeavor to ensure no harm whether physical or emotional befalls on you as a result of your participation in the study.

Participation to this study is voluntary. You have a right to refuse to participate without fear, intimidation or penalty. You also have the liberty to withdraw from the study any time you feel like.

If you require more clarification of the abovementioned please do not hesitate to contact me. My contacts number is 0724542364 or you can contact me through my email address matoarchitect@yahoo.com.

I hereby acknowledge that have discussed the above with the subject. It is of my point of view that the subject has comprehended the information given him/her.
Researcher signature_____ Date_____

I understand the above and hereby, freely consent to take part in this study and that my participation is voluntary and that I may refuse to participate or withdraw anytime without penalty.

Subject's signature_____ Date_____

Witness' signature_____ Date_____

Researcher's signature_____ Date_____

APPENDIX B: QUESTIONNAIRE

Part A: Socio-demographic factors

1. What is your age (years)?

☐ <20
☐20-29
☐30-39
☐40-49
☐50-59
☐Above 60

2. What is you level of education?

☐None
☐ Primary
☐Secondary
☐Tertiary

3. What is your marital Status?

☐Single
☐Married
☐Divorced
☐Widowed

Part B: Stage of disease

4. What is the FIGO stage of the cancer at diagnosis?

☐Stage 0
☐Stage 1
☐Stage 2
☐Stage 3
☐Stage 4

Part C: Mode of financing

5. What mode of payment used to pay for the radiotherapy sessions?

☐ Out of pocket
☐ National Health Insurance Fund
☐ Private Insurance
☐ Community based health insurance

Part D: Treatment time

6. What the approximated time of treatment (in days)?
☐ Days
7. Number of days completed
☐ Days

Part E: Side effects of radiotherapy

8. What were the reported side effects due to radiotherapy?

☐ Urological
☐ Cutaneous
☐ Neurological
☐ Others specify……