PREVALENCE OF CERVICAL CYTOLOGICAL ABNORMALITIES AND HUMAN PAPILLOMA VIRUS INFECTION AMONG RENAL TRANSPLANT RECIPIENTS AT KENYATTA NATIONAL HOSPITAL

Dissertation submitted in part fulfillment of the requirements for the degree of Master of Medicine in Obstetrics and Gynaecology at University of Nairobi.

By

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H58/69081/2011

DEDICATION

This book is dedicated to my parents, Albert and Mary, and my siblings Newton, Eva, Chuli and Joan for their unwavering support.

DECLARATION

This is to declare that this research work and dissertation is my original work and that it was done with the guidance of my supervisors. It has not been submitted to any other university for the award of a degree.

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LIST OF ABBREVIATIONS

ASCUS:	Atypical squamous cells of undetermined significance
CKD:	Chronic Kidney Disease
CIN	Cervical Intraepithelial Neoplasia
CIS	Carcinoma in situ
DM	Diabetes Mellitus
DNA	Deoxyribonucleic acid
ESRD	End stage renal disease
HAART	Highly active antiretroviral therapy
HIV	Human Immunodeficiency Virus
HPV	Human Papillomavirus
HrHPV	High risk human papillomavirus
HSIL	High grade squamous intraepithelial lesion
LSIL	Low grade squamous intraepithelial lesion
LEEP	Loop Electrosurgical Excision Procedure
LrHPV	Low risk human papillomavirus
Rb	Retinoblastoma gene
RTRs	Renal transplant recipients
RNA	Ribonucleic acid
STI	Sexually transmitted Infections
TB	Tuberculosis
TGFb	Tumor growth factor beta

GLOSSARY OF TERMS

ASCUS	Atypical squamous cell of undetermined significance. A category of abnormal cervical cells according to the Bethesda system of classification of cervical abnormalities.
CIN	Cervical Intraepithelial Neoplasia, also called dysplasia, is a disordered growth and development of the epithelial lining of the cervix. It is divided into various degrees depending on severity such as CIN I, CIN II and CIN III.
CIN I	Mild dysplasia. Disordered growth involving lower third of epithelial lining.
CIN II	Moderate dysplasia involving 2/3 of the epithelial lining.
CIN III	Severe dysplasia involving more than 2/3 of the epithelial lining.
CIS	Carcinoma in situ. Full thickness dysplasia.
DNA	Deoxyribonucleic Acid. A neuclotide chain containing bases that make a double helical structure that carries the genetic code.
HPV	Human Papillomavirus. A DNA virus that is causative agent for CIN and most invasive cancer
HSIL	High grade squamous intraepithelial Lesion is high grade changes of the cervical cells which have high probability of progressing to invasive cervical cancer
LSIL	Low grade squamous intraepithelial lesion low grade changes immediately after normal cervical cells have been infected by HPV virus and they start changing towards cancer.
ICC	Invasive cervical carcinoma.

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ABSTRACT

Background

Renal transplant began in the 1950's. Over the years more specialists have been trained and as a result more transplants are done each year and with the improved post transplant care and immunosuppressant therapy, these patients have longer survival rates. As a consequence of this, a resurgence of latent forms of viral infections occurs, in this regard human papillomavirus, leading to an upsurge of anogenital malignancies such as cervical cancer, vulval cancer and anal cancer. The risk of cervical cancer increases by 14 fold in renal transplant recipients yet this can be prevented with more vigilant cervical cancer screening. Early detection of precancerous lesions can lead to timely treatment and reduce the burden of disease that may occur as a result of multiple illnesses. Owing to the multiplicity of complications associated with renal transplant, cervical cancer screening may take a back seat in this population. This study will determine the prevalence of HPV and cervical cytological abnormalities in the renal transplantation population in a bid to emphasize the need for yearly cervical cancer screening.

Broad Objective

The main objective of this study was to determine the prevalence of cervical cytological abnormalities and HPV infection in renal transplant recipients at KNH.

Methods

This was a cross-sectional study to determine the prevalence of cervical cytological abnormalities and HPV infection among renal transplant recipients. Data collection was done by the principal investigator and individuals were identified through consecutive sampling. A consent form was filled followed by administration of a structured questionnaire to assess the socio-demographic, reproductive and clinical history of participants. Thereafter, a pap smear and liquid based cytology sample for collection of HPV was done. Data was analysed using SPSS version 22, t-test and chi test for the continuous and categorical variables, Fischer's test and chi square was used for associations.

Results

Thirty two female renal recipients who met the eligibility criteria were enrolled into the study. There median age was 38.5 years (range 24-64 years). The mean duration since transplant was 4.89 years (SD 5.15). The prevalence of hrHPV infection was 33% (10/32) whereas the prevalence of abnormal cervical cytology was 12.5% (4/32)). The marital status, parity and lifetime number of partners were found to be statistically significant

Conclusion

The prevalence of premalignant cervical lesions and hrHPV infection was found to be high among female renal transplant recipients attending the post transplant clinic at KNH. Though few, these findings raise awareness of the magnitude of this problem among this population. The use of immunosuppressive therapy is also inevitable, however health awareness measures aimed at preventing the acquisition of HPV and other STIs as well as reduction in the number of sexual partners will greatly impact on the occurrence of HPV and subsequent premalignant cervical lesions in this population. Moreover, these findings should generate interest for future studies in order to engage best practices in screening and managing premalignant cervical lesions among renal transplant recipients.

CHAPTER 1:

INTRODUCTION AND LITERATURE REVIEW

1.1 Introduction

Cancer of the cervix is the fourth most common cancer among women worldwide accounting for 527,624 new cases in 2012. About 86% of these cases occur in developing countries, representing 12% of all female cancers. In Africa, cervical cancer is the second most common after breast cancer whereas in East and Central Africa it is the leading cause of cancer in women. Kenya has a female population of 10.32 million over 15 years of age who are at risk of developing cervical cancer. It is currently estimated that of these women, 4802 are diagnosed with cervical cancer every year[1]. Moreover, the mortality associated with cancer of the cervix is 265,653 deaths globally. It is also ranked as the commonest cause of mortality followed by breast cancer. Annual deaths in East Africa due to cancer of the cervix is 28,197 while that of Kenya is 2541, showing that more than half of the newly diagnosed cases are likely to die yet this disease is preventable[1]. Early detection of precancerous and cancerous lesions of the cervix is the best way to reduce the morbidity and mortality associated with the disease, however lack of structured screening programmes, inadequate financial and human resources, inadequate health infrastructure, coupled with the low awareness of cervical cancer and socio-cultural beliefs, are barriers to its prevention. Moreover, the high poverty levels have led to the high prevalence of cervical dysplasia and cervical cancer[2, 3].

Cervical cancer development is a sequel of precursor cervical intraepithelial neoplasia(CIN). The natural history of disease progression is intertwined with HPV infection[4]. Human Papillomavirus is a small non enveloped double stranded DNA virus that is very host specific[5]. It is the most

prevalent sexually transmitted disease today with about two thirds of young adults acquiring HPV infection within the first two years of sexual activity[6]. Over100 types of HPV have been identified based on their DNA sequence. Each of these has either cutaneous or mucosal tropism: forty of those with mucosal tropism affect the anogenital system causing different disease manifestations. Based on the oncogenicity, HPV has been divided into high risk and low risk. The high risk HPV is associated with malignancy whereas the low risk HPV are known to cause benign lesions such as warts. The high risk HPV includes 16, 18, 31, 33, 45, 51, 52, 56, 58, 59, 68, 73 and 82. Of these, HPV 16 and 18 have been shown to cause 70% of all cervical cancers worldwide with 16 being the most common. HPV 31,33, 35 and 45 are found in 2-4% of invasive cervical cancer[5, 7].

The pathogenesis of cervical cancer is linked to HPV infection and involves four stages. It begins by infection of the metaplastic epithelium in the transformation zone of the cervix by HPV through microabrasion, a common occurrence in young females who are sexually active. By lateral extension of the basal cells, healing of the microabrasion occurs and by so doing allows entry of the HPV into the cell nucleus. Once HPV has entered a cell, it can coexist in two biological forms, the non-productive infection also called latent phase and the productive phase. In the latent phase, HPV DNA resides in the cells and replication occurs only in concert with replication of the host chromosomal DNA. In the productive infectious phase, viral replication occurs independent of host chromosomal DNA resulting in production of a large number viral DNA. This occurs in the suprabasal layer. However, most of these infections clear as a sequel of a good cell mediated immunity in majority of individuals; about 90% resolve. Clearance varies from between 5 to 6 months for low risk HPV and 8 to 14 months in those with high risk HPV. When the immune system is compromised, there is poor clearance of HPV leading to persistence

of the virus in epithelium. This prolonged latent phase in immunocompromised individuals is what leads to disease progression. The suprabasal cells do not naturally express the replication machinery required that the virus requires for survival. As such, through its capsid proteins E6 and E7, the virus is able to prolong its cell proliferation. E6 and E7 block the negative regulators of the cell cycle, p53 and Rb (Retinoblastoma) gene. P53 and Rb gene protects genome integrity by forcing apoptosis or inducing cell cycle arrest until errors in DNA replication can clear. Viral load integration and genetic predisposition have been also shown to influence the persistence of the virus. Once the epithelium has been persistently exposed to HPV, precancerous cervical lesions develop and eventual invasion of the basement membrane leads to cervical cancer[5, 7, and 8].

The main risk factor in the causation of cervical cancer is sexual activity. Herein lies the number of lifetime and recent sexual partners and age at first coitus. Other risk factors include HPV viral type, viral load and co-infection with other viral serotypes, smoking, use of oral contraceptives, multiparity, presence of sexually transmitted diseases such as Chlamydia trachomatis and Herpes Simplex virus, chronic inflammation and immunosuppressive conditions both innate and acquired such as HIV. The use of immunosuppressive therapy in chronic conditions such as inflammatory bowel disease and organ transplant recipients this includes renal transplant recipients is also a risk factor[9, 13].

RTRs are therefore in an immunosuppressed state similar to HIV patients[10]. Just like with the improvement with care of HIV patients due to advent of HAART, there has been remarkable improvement in the post-transplant care of RTRs and advances in treatment regimes offered post renal transplant thus prolonging the survival rates of RTRs[11]. Consequently, with the long survival rates, the occurrence of post transplant malignancies has increased tremendously with the incidence estimated to be between 15% to 20 % after 10 years of immunosuppressive therapy

and that of cervical cancer to have increased by 14 fold. Projections over the next 20 years show that cancer will be the leading cause of mortality in RTRs taking over from post operative complications[12]. Therefore early detection of HPV infection is key in the prevention of cervical dysplasia and cervical cancer in RTRs.

Prevention of precancerous and cancerous lesions of the cervix aims at knowing the risk factors and the disease progression. Primary prevention aims at reduction of HPV infection while secondary prevention aims at early detection and treatment of precancerous cervical lesions. The two main methods of primary prevention are behavioural modification methods that aim at reduction of HPV exposure and HPV vaccination. Secondary prevention aims at early detection of precancerous lesions of the cervix and involves cervical cytological screening methods and HPV DNA/RNA testing[13]. In RTRs it will reduce the burden of disease that occurs as a result of the multiple diseases caused by chronic renal disease by offering timely treatment. Treatment modalities of precancerous cervical lesions include either ablative methods or excisional methods.

1.2 Literature review

It is well documented that cervical cancer is a sequel of precancerous cervical lesions and that HPV is known to play a pivotal role in this development though less than 1% of those infected with HPV progress to develop invasive disease[14].

The prevalence of cervical dysplasia in Kenya is estimated to be between 2.56% and 16.7%[15, 16, and 17]. The distribution of cervical dysplasia also varies with LSIL having a prevalence of 7%, HSIL 6.8% and ICC 0.23% as shown by a study done in a family planning Clinic in Nairobi between 1998 and 2000[18]. Geographical distribution of HPV varies from region to region with

the rates estimated to be between 1.4% and 25.65% in asymptomatic women[19]. The prevalence of HPV in African countries is estimated by The World Health Organisation to be approximately 22% whereas that of Kenya is approximately 39.6% in asymptomatic women. HPV type 16 and 18 was found in 9.1% with normal cytology, 20.9% with LSIL, 39.5% with HSIL and 69.4% in those with invasive cervical carcinoma. HPV type 45 was noted to have a high prevalence of 18.3% in Kenya compared to the world's prevalence of 4.4%[20].

The age distribution of cervical dysplasia and HPV shows a bimodal peak. The first is soon after initiation of sexual activity with a peak prevalence of 26-30 years and a second peak between 45 and 50years. CIN 2/3 lesions were noted 5 to 15 years after the first peak while ICC was noted more than 15 years after the first peak. This age distribution forms the basis for an increased need for cervical cancer screening even beyond the reproductive period.[21].

Chronic kidney disease (CKD) is of public health concern too. The Global Burden of disease ranked it 27th in the list of causes of total number of global deaths in 1990, but rose to 18th in 2010[22].Kenya's population at 38.6 million has an estimated prevalence of end stage renal disease of 15.6 per million population[23]. CKD invariably progresses to ESRD, a condition that requires dialysis but improves with renal transplant. In the East African region, Kenya has pioneered in the renal transplant carrying out approximately 20 transplants per year. RTRs are put on combined immunosuppressive therapy such as steroids, calcinerium inhibitors, and proliferative signal inhibitors among others in order to reduce rejection. However this reduces their immunity remarkably to a state similar to patients with HIV. As a result of lowered immunity, an upsurge of viral infection related malignancies occurs. Of note is Kaposi's sarcoma, skin cancer and HPV related cervical dysplasia and cancer[24]. In RTRs, the incidence of occurrence of all malignancies is estimated to be between 15% and 20% after 10 years of treatment. Moreover, cancer has been

shown to be the second leading cause of death in this population and it is expected that the mortality due to cancer will be moved to first cause of death in the next two decades[12].

Among transplant recipients, cancer of the cervix accounts for 3% of all malignancies. In RTRs the risk of development of cervical intraepithelial neoplasia increases by 14 fold while that of invasive cervical cancer increases by 3.0 to 8.6 fold whereas that of HIV shows a 2-22 increase in cervical cancer development[24, 25, 26] .

Several studies have been carried out to assess the incidence of occurrence of cervical intraepithelial neoplasia and HPV among RTRs. Poreco et al described a 14 fold increase in the incidence of cervical dysplastic lesions in RTRs as compared to an age matched control group[27]. Halpert et al studied 105 RTRs and found 17.5% to have HPV infections as evidenced by presence of koilocytes in cervical smears and biopsies and 9.5% had lower genital neoplasia. The rate of viral infections was 9 times greater than the general population and 17 times greater in a matched immunocompetent population[28]. Seshadri et al did a prospective study on 42 RTRs of 41 years of age and compared them to parity matched controls. They examined biopsies and found 24 had evidence of HPV and 10 had SIL in the RTRs group whereas in the control group, 13 had evidence of HPV while only 3 had SIL. The Odds ratio being 6.1 and the severity of dysplasia was noted to be more in the RTRs group[29].

The prevalence of HPV and CIN in renal transplant recipients has also been compared to different groups. Fairley et al compared it with dialysis dependent individuals and patients with renal impairment. They found the prevalence of cervical abnormalities was not detected in those with low renal impairment while that of the dialysis dependent (12.4%) and RTRs (13%) was

almost similar. However, the prevalence of HPV was slightly higher with the low renal impairment having 4.5%, dialysis dependent 20% and RTR 15%[30].

Unlike RTRs, HIV has been extensively studied. Consequently, data in this subgroup is widely available. In a review by Denny L.A. et al on HPV, HIV and immunosuppression, they found that the prevalence and persistence of HPV infection was higher in the HIV positive group as compared to the HIV negative group. Of note is that the HIV positive group was more likely to have more than one HPV subtype isolated. This result was attributed to the fact that HIV positive patients have an impaired cell immunity which increases the chances of getting HPV infection partly because both HPV and HIV are sexually transmitted diseases. There is also a reduction in the capacity of the immune system to clear the HPV infection and the reactivation of latent HPV infection, both factors contributing to progression into cervical dysplasia also in RTRs[31].

Studies have been done to compare the incidence of occurrence of malignancies between HIV patients, organ transplant patients and the general population. De Morais et al in a meta-analysis found that the Standardized Incidence Ratio was high for both the HIV patients and the organ transplant recipients than in the general population[32].Similarly, in a population based cohort study by Vajdic et al, they found that the incidence of most cancers increased only slightly after dialysis but increased by more than twofold after renal transplant. These studies show the important role of interaction between the viral infections and immune system in the etiology of cancer occurrence[26].

Cervical cancer screening still remains the mainstay of prevention even in the renal transplant population. Various screening methods are employed in order to detect these lesions early and therefore offer timely diagnosis and treatment. Cervical cytology has been the standard of

secondary prevention. In countries like Finland, Denmark, Iceland and Sweden where cervical cytological programmes were implemented in the 1960's, the incidence has reduced by over 50%[33]. In our set up, with limited resources both financial and human, VIA/VILI has formed an inexpensive alternative method of screening[34]. HPV DNA/RNA detection methods have been developed as a result of the strong causal relationship to occurrence of cervical cancer. Though expensive, this method has been shown to have higher sensitivity and a high negative predictive value when compared to the other screening methods. It has also been shown to be a better method of follow up in patients with recurrence[35].

1.3 Justification

More renal transplants are being performed worldwide owing to the increased expertise and the improved facilities in this field. In Kenya, approximately 20 renal transplants are done annually. Females are amongst those that have benefited from this; most of who are in the reproductive age and whose sexual function may have improved with the renal transplant.

Moreover, with the advent of the current combination immunosuppressive therapy, the survival rates post renal transplant has improved remarkably and studies are now showing that the occurrence of post-transplant malignancies such as cervical cancer may increase with the prolonged use of these drugs. The occurrence of comorbidities most commonly the non communicable diseases such as diabetes and hypertension, among RTRs is not uncommon thus necessitating frequent hospital visits. Despite this frequency, the cervical cancer screening rate has been shown to be low.

There is a paucity of data on the prevalence of precancerous cervical lesions and HPV infection in the post renal transplant population in Africa.

This study sought to determine the prevalence of precancerous cervical lesions and HPV in the RTRs in KNH and ascertain the need for an integrated approach between the gynaecologists and renal physicians in the management of RTRs in order to provide better prevention methods and holistic treatment and follow up plans for management of precancerous cervical lesions.

1.4 Research question

What is the prevalence of cervical cytological abnormalities and HPV infection among renal transplant recipients at KNH?

1.5 Objectives

1.5.1 Broad Objective

To determine the prevalence of cervical cytological abnormalities and HPV infection among renal transplant recipients at KNH.

1.5.2 Specific Objectives

Among renal transplant recipients attending the post renal transplant clinic at KNH,

1. Determine the prevalence of cervical cytological abnormalities.
2. Determine the prevalence of HPV infection
3. Determine the socio-demographic and clinical characteristics associated with abnormal cervical cytology and HPV infection.

CHAPTER 2

METHODOLOGY

2.1 Study Design

This was a descriptive cross-sectional study. It was appropriate in order to calculate prevalence and possible significant associations between variables. The study population was female post renal transplant recipients attending the post transplant clinic at KNH. Data on HPV and Pap smear cytology (dependent variables) were used to calculate their prevalence in the study population while independent variables were analysed to determine any associations with these two. The study was carried out between July to November 2014.

2.2 Study Site

The study was undertaken at the renal post-transplant clinic in Kenyatta National Hospital. The post-renal transplant clinic is carried out in the renal unit and is run every Tuesday morning between 9a.m and 1p.m. This unit has a wide catchment of renal post transplant patients on follow up from within Kenya and also East Africa.

2.3 Study Population

All females who attended the post-renal transplant clinic within the study period were invited to participate in the study after meeting the eligibility criteria.

2.4 Respondent Selection

Inclusion Criteria

a) Females>18 years of age who had undergone renal transplant and had been on immunosuppressive therapy for more than 6 months and were able to give informed consent.

Exclusion criteria

a) Females who had undergone total abdominal hysterectomy
b) Patients with confirmed cervical cancer or invasive cervical carcinoma.

2.5 Sample Size Calculation

Of the two outcomes to be used in the study i.e. CIN prevalence and HPV prevalence the estimated prevalence based on recent studies are 3.6%[26] and 25.5%[36], respectively. The total number of female renal transplant patients available at KNH during the six month period (study period) is 50. Therefore, Fishers formula for estimating sample size in prevalence studies with a finite population correction was used to estimate the sample size accounting for the limited number of potential subjects undergoing renal transplant at KNH (maximum N = 50 during study period).

$$\boldsymbol{n = \frac{NZ^2P(1-P)}{d^2(N-1)+Z^2P(1-P)}}$$

N = Total population of renal transplant recipients estimated at 50 women in KNH during the proposed study period

P = Prevalence of CIN in female renal transplant recipients as reported by Meuwiss et al in 2010

1-P = 1 minus the CIN prevalence in female renal transplant patients

Z = Z statistic representing 95% level of confidence (1.96)

d = desired level of precision set to 1.8% for CIN prevalence of 3.6%

$$n = \frac{50 \times 1.96^2 0.036(1 - 0.036)}{0.018^2(50 - 1) + 1.96^2 \times 0.036(1 - 0.036)}$$

n = 45

Using the same number of patient (n = 45) and the formula presented above, and the more common prevalence of HPV it was determined that using a HPV prevalence of 25.5% the sample size of 45 could estimate HPV prevalence with an acceptable precision of 4.5%. Therefore the minimum number of patients will be 45.

2.6 Data collection methods and procedure

Recruitment and consenting procedure

Specimens taken

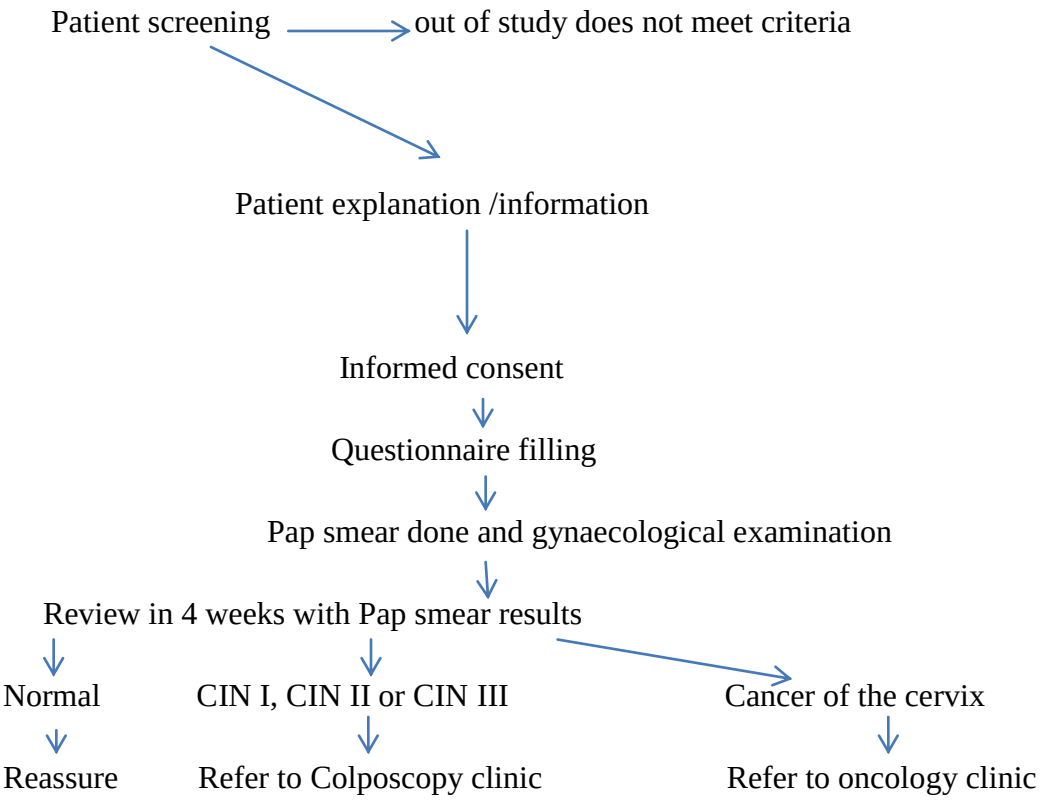
Conventional Pap smears

Liquid based cytology (Thin Prep) specimens

Materials/Tools

Questionnaires, pens, private room, sterile normal saline, cervical brushes, speculums, Pap smear kit, LBC specimen bottles and a light source.

Study flow chart



Procedure

Consecutive selection of women with renal transplant attending renal post-transplant clinic were approached by the principal investigator and invited to participate in this study. A detailed explanation of the study- its purpose, procedure, benefits and risks was provided. Participants were then informed that part of the samples would be exported to Manchester for analysis.

Consenting

A written consent was obtained from eligible participants. After obtaining consent, a questionnaire was administered to the patient/client that assessed the socio-demographic and

clinical characteristics of the client. It also helped to explore the patients future cancer screening use, knowledge and misconceptions associated with Pap smear procedure. This was done in a private room at the renal clinic. Once this was done, the Pap smear was collected on those who met the eligibility criteria.

Pap smear

A pap smear is a screening test in which a sample of cells from a woman's cervix is collected and smeared on a microscope slide and fixed with ethyl alcohol. It is used in gynaecology to detect premalignant and malignant processes in the cervix. It was invented by George Papanikolau.

Once a slide is fixed, it is immersed in three stains each of which stains differently for different cells and different parts of a cell. Haematoxylin stains nuclei blue; EA 36 stains cytoplasm of immature cells as greenish blue, and that of mature cells as pink. Orang-G stains keratin orange in colour.

Before the Pap smear was done, a gynaecological examination was performed on the client.

Procedure:

A pap form was filled. The materials to use were shown to the patient and an explanation given. The pap kit as well as the thin prep cytology specimen bottle for HPV DNA testing was labelled and a serial number given.

The patient was asked to undress and lie on a couch. The Principal investigator then put on the gloves. The speculum was lubricated with warm water. Then the external genitalia was parted and speculum inserted, and then opened to visualize the cervix.

The cervix was examined for any abnormalities such as inflammation, discharge, warts or masses noted. Discharge was wiped off using a cotton swab. The cervical brush was then inserted so as to take a sample of both the endocervix and ectocervix and rotated 3 to 5 times. The brush was rubbed on the slide and ethyl alcohol used to fix the slide. The slide was then air dried. The same brush will be dipped in the thin prep specimen bottle and swirled several times. The bottle was then tightly closed.

The conventional pap smear samples were assessed locally by a cyto-pathologist. However, the liquid based cytology samples were sent to Manchester for HPV DNA testing.

Pap smear results were reported using the Bethesda classification by the cyto-pathologist. Results were obtained within a month recorded in the results form and given to the patients.

HPV DNA testing

All Thin Prep liquid based cytology samples were sent to Manchester and analysed by staff trained and certified by Hologic. HPV testing of LBC samples was carried out using the FDA-approved Cervista HPV HR test in conjunction with the Cervista MTA (Hologic) automated platform according to the manufacturer's instructions. This system provides ultra-pure DNA extraction and HPV testing in one sealed unit requiring no user input following initiation. Cervista uses three oligonucleotide mixtures designed to detect 14 high risk HPV types within three familial groups based on phylogenetic similarities: Mix 1 detects types 51, 56, and 66; Mix 2 detects types 18, 39, 45, 59 and 68; Mix 3 detects types 16, 31, 33, 35, 52, and 58. A separate human histone 2 gene probe serves as an internal control for cellular DNA content within the LBC sample. The A HPV positive signal is indicated by fluorescent signal above an empirically derived cut-off value. Results were obtained within a month, recorded in the results form and given to the patients.

2.7 Data collection/management

Data collection

Data was collected by the principal investigator who ensured that the standard procedure of collection was observed. The questionnaire was tested outside the study period in order to determine its applicability. It was examined for clarity, ambiguity, time taken to fill it out and analyzability. Appropriate adjustments were then made. The Principal investigator introduced herself to the study participants and the purpose of study was explained. Ultimate benefits to the patients were stressed upon after which an informed consent in English/Kiswahili was signed (Appendix I or II). The questionnaire was filled by the researcher together with patient in a private room to ensure confidentiality. During the interview, bilateral conversations were encouraged. All the information collected was entered in the questionnaire. All specimen collected were stored in a safe place awaiting transfer to the cyto-pathologist.

Once results were availed, approximately 4 weeks, there was a discussion with the patient. Depending on the results, further management was provided. Those that needed referral to the KNH colposcopy clinic had the form filled out and handed to them.

Quality control and assurance procedures

Pre-analytical

There was pre-testing of the pre-designed questionnaire before actual data collection commenced outside the study period. Feedback obtained was used to make the necessary changes in the questionnaire that formed the final draft for use by the research participants. In order to avoid double recruitment, the participants' file numbers was entered in a register upon recruitment for serialization. This register was counter checked on a regular basis for any double entries.

Cervical specimens were collected by the principal investigator herself to ensure that the standard procedure of collection was observed. Samples were given a unique number, labeled and stored in a safe locker awaiting transportation to the laboratories.

Analytical

Laboratory forms accompanying the participant's specimens were labeled using the unique numbers. This was counterchecked at the laboratory to ensure correspondence. The standard procedure for staining of the pap smears was done.

To ensure utmost quality of the Pap smear results, 10% of the slides were re-examined by a different cyto-pathologist who had no access to the prior results provided by the first cyto-pathologist.

The Cervista HPV HR test has an internal control that determines the relative quantity of sample DNA in each reaction. Sample results are valid when both positive and negative controls yield correct results. A positive result indicates that at least one of the 14 high risk types is present in the DNA sample.

Post-analytical

Recording of the results to the questionnaire was carefully done to ensure correspondence between assigned unique numbers, laboratory numbers and client's questionnaire.

Data management

Data generated from the study was stored in a password protected computer and backed up on an external hard drive which was under the safe custody of the principal investigator. Each entry had a unique number in order to maintain the participants' confidentiality. The data collection

questionnaires were filled and stored in a safe cabinet where verification of results can be done whenever necessary. The data was entered into an MS access database by the statistician and exported into a Statistical Package for Social scientists version 21 (SPSS, Chicago) which was used for data analysis.

2.8 Data Analysis

Descriptive analysis of socio-demographic variables was conducted by calculating mean and standard deviation for continuous variables like age and determining frequency distribution for categorical data e.g. sex, and socio-economic status. The prevalence of HPV infection and CIN was calculated as proportion of subjects with positive HPV and CIN investigation findings. Cross tabulations was used to examine the distribution of HPV infection according to the patients' demographic and clinical characteristics. Similar analysis was also conducted for patients with positive CIN findings. Chi square and Fisher's exact test was used to compare associations between HPV and CIN prevalence and patient demographic or clinical characteristics.

2.9 Ethical consideration

Approval for the study was obtained from the KNH/UON ethical review committee and the Ministry of Health before any study procedures were implemented. Each client gave a written, non-coerced informed written consent after a detailed explanation of the study purpose, procedure, benefits and risks provided by the interview in a language they could understand. All clients were informed that part of the samples collected would be exported to Manchester for analysis and that the samples would solely be used for this study. Patients were not denied access to appropriate management of their illness as per hospital protocol. All information was strictly

confidential. The clients did not pay for the Pap smear. Once specimens were collected, approval was then sought from ERC for shipment of samples. On receipt of the results, appropriate treatment was offered. Each patient had their results given individually and a follow up plan explained. Those that required referral were sent to the appropriate clinics.

CHAPTER 3

RESULTS

3.1 Study Participants Characteristics

A total of 44 female post-transplant recipients were approached. Of these, 9 did not meet the inclusion criteria and 3 declined to participate in the study. Therefore, 32 female participants met the inclusion criteria and participated in the study. The results will be presented based on each specific objective. Table 1, 2 and 3 below describes the socio-demographic, reproductive and clinical characteristics of the study population.

Socio-demographic characteristics

Table 1: Socio-demographic characteristics of female renal transplant recipients at KNH

Socio-demographic factors	**Freq.(Percent)**
Age (in years) Mean/SD	**41.88/ 12.89**
20 – 29	7(22)
30 – 39	9(28)
40 – 49	5(16)
>50	11(34)
Marital Status	
Married	20(62.5)
Single	8(25.0)
Separated/Divorced	2(6.3)
Widowed	2(6.3)
Religion	
Catholic	4(12.5)
Protestant	28(87.5)
Level of Education	
Primary	1(3.1)
Secondary	9(28.1)
College/University	22(68.8)
Occupation	
Self employed	4(12.5)
Formal Employment	12(37.5)

Business	9(28.1)
Student	1(3.1)
Unemployed	6(18.8)
Socio-economic status	
Low (earn < Ksh. 10, 000 p.m.)	7(21.9)
Middle (earn between KShs. 10, 000-30,000 p.m.)	3(9.4)
High (earn >KShs. 30, 000 p.m.)	22(68.8)
Usual residence	
Rural	5(15.5)
Urban	26(81.3)
Foreigner	1(3.1)

Table 1 above describes the socio-demographic characteristics of the study participants. Their mean age was 41.88 years with 62.5% (20/32) of them being married. There were no Muslims in the study; however, 87.5% (28/32) were Protestants. Majority of them had acquired at least a secondary level of education, with 68.8% (28/32) having attained a form of tertiary education. Only 7 of the 32 participants had no regular source of income with 68.8% being high income earners. There was one foreigner who attended the post-transplant clinic.

Reproductive characteristics

Table 2: Reproductive characteristics of renal transplant recipients at KNH

Variable	**Frequency/ (Percent)**	**Mean**	**SD**
Age at menarche		**14.5**	**1.53**
<15years	19(59.4)		
>15 years	7(21.9)		
Cannot remember	6(18.8)		
Age at first sexual intercourse		**20.16**	**3.00**
Before 14 years	2(6.3)		
15-17	4(12.5)		
18-21	14(43.8)		
22-24	10(31.3)		
>24 years	1(3.1)		

Cannot remember	1(3.1)		
Number of lifetime sexual partners		**1.75**	**1.016**
1	18(56.3)		
2	6(18.8)		
3	7(21.9)		
4	0(0)		
5	1(3.1)		
Parity (Term pregnancies)		**1.97**	**1.694**
Nulliparous	8(25)		
1	6(18.8)		
2	8(25.0)		
3	3(9.4)		
4	3(9.4)		
5	4(12.5)		
History of STI			
Yes	2(6.2)		
No	30(93.8)		
Current contraceptive use			
Yes	4(12.5)		
No	28(87.5)		

The mean age of menarche of the study participants was 14.5 (SD± 1.53) years whereas the mean age at first sexual intercourse was 20.16(SD± 3.00) years with 74.2% (23/31) having their first sexual encounter after 18 years of age. Moreover, 56.3% (18/32) had one lifetime sexual partner with 75% of the study participants having given birth at least once with a mean parity of 1.97 (SD± 1.69) and only 9.38% (3/32) study participants ever having had an abortion. Of note is that only 12.5% (4/32) of the participants were on any form of contraceptive during the study period. Of the 4 participants, one had a bilateral tubal ligation and the rest were using condoms as contraceptive options. Only 2 (6.25%) of the study participants reported a history of STD. None of the study participants had ever used cigarettes. Table 2 above shows the reproductive characteristics of the study population.

Clinical characteristics

Table 3: Clinical characteristics of female renal transplant recipients at KNH

Variable	Frequency/ (Percent)	Mean	SD
1. Age at onset of CKD		**33.16**	**14.126**
i. <20years	5(15.6)		
ii. >20years	27(84.4)		
2. Duration of CKD		**3.84**	**3.845**
i. <5 years	28(87.6)		
ii. >5 years	4(12.4)		
3. Underlying cause of CKD			
i. Hypertension	23(71.9)		
ii. Diabetes	5(15.6)		
iii. Chronic Glomerulonephritis	1(3.1)		
iv. Infections	1(3.1)		
v. Connective Tissue Disorder	2(6.3)		
4. Number of transplants		**1.09**	**0.296**
i. One	29(90.6)		
ii. >one	3(9.4)		
5. Immunosuppressive therapy			
i. Cyclosporine+Mycophenolate mofetil+steroid	12(37.5)		
ii. Tacrolimus+Mycophenolate mofetil+Steroid	12(37.5)		
iii. Cyclosporine+Azathioprine+Steroids	1(3.1)		
iv. Tacrolimus+Azathioprine+ Steroids	2(6.3)		
v. Others	5(15.6)		
6. Duration of immunosuppression		**4.89**	**5.15**
1. <2years	15(46.9)		
2. 3-5years	10(31.3)		
3. 6-10years	2(6.3)		
4. >10years	5(15.6)		
7. Creatinine levels(Graft function) µmol/L		**93.37**	**27.71**
1. 50-60	1 (3.1)		
2. 61-70	2 (6.3)		
3. 71-80	8 (25)		
4. 81-90	8(25)		
5. 91-100	6(18.8)		
6. >101	7(21.9)		

Table 3 above describes the clinical characteristics of the study participants. The mean age at onset of CKD was 33.16years (range 7-59 years). More than three quarters of the study participants (87.6 %) had CKD for a period of less than 5 years before renal transplant was done. Hypertension and Diabetes contributed to 87.5% of the causes of CKD. One study participant was noted to have developed CKD due to SLE nephritis and another IgA nephropathy. Three of the participants (9.38%) had reported an episode of rejection and had second transplants done. The mean creatinine level post-transplant was 93.38µmol/L. The most common combinations of immunosuppressive therapy at 37.5% each were Cyclosporine + Mycophenolate mofetil+ steroid and Tacrolimus+Mycophenolate mofetil + steroid. The median duration of immunosuppression was 3 years, with 78.1% of the study participants having been on immunosuppresants for <5 years.

3.2 Prevalence of abnormal cervical cytology

Out of 32 renal transplant recipients screened, 4 had abnormal cervical cytology giving a prevalence of 12.5% (95% CI: 0.39% - 24.61%). Table 4 below shows the distribution.

Table 4: Distribution of cervical dysplasia among the study participants

Cervical cytology	Freq./Percent
Normal	28(88)
HSIL	0(0)
LSIL	2(6)
ASCUS	1(3)
AGC	1(3)
ASC-H	0(0)
ICC	0(0)
Total	**32(100)**

(HSIL- High grade intraepithelial lesion, LSIL-Low grade lesions, ASCUS- atypical squamous cells of undetermined significance, ASC-H- atypical squamous cells likely high grade, AGC- atypical glandular cells, ICC-invasive cervical carcinoma).

3.3 Prevalence of HPV infection

Of the 32 patients that were screened, 10 tested positive for high risk HPV infection giving a prevalence of 31.3% (95% CI: 14.3% -48.2%). In our study however, we only analysed for the hrHPV subtypes as a group but did not report for the individual subtypes.

3.4 Relationship between socio-demographic characteristics and cervical cytological findings among renal transplant recipients

Table 5: Socio-demographic characteristics associated with cervical cytology findings among renal transplant recipients at KNH

	Cervical cytological abnormalities		
Socio-demographic characteristics	**Normal**	**Abnormal**	**P value (Fischer's Exact test)**
	Freq./ Percent	**Freq./ Percent**	
1. Age (in years)			
20 – 29	7(24)	0(0)	**0.352**
30 – 39	7(24)	2(50)	**0.057**
40 – 49	4(17)	1(25)	**0.488**
>50	10(34)	1(25)	**0.573**
2. Marital Status			
Married	20(69)	0(0)	**0.136**
Single	7(24)	1(33)	**0.746**
Separated/Divorce	0(0)	2(67)	**0.012**
Widowed	2(7)	0(0)	**0.762**
3. Religion			
Roman Catholic	4(14)	0(0)	**0.569**
Protestant	24(86)	4(100)	**0.569**
4. Level of Education			
Primary	1(4)	0(0)	**0.875**
Secondary	8(29)	1(25)	**0.689**
College/University	19(68)	3(75)	**0.632**
5. Occupation			

Self employed	3(11)	1(25)	**0.431**
Formal	10(36)	2(50)	**0.485**
Business	9(32)	0(0)	**0.246**
Student	1(4)	0(0)	**0.875**
Unemployed	5(18)	1(25)	**0.584**
6. Socio-economic status			
Low	6(21)	1(25)	**0.648**
Middle	3(11)	0(0)	**0.660**
High	19(68)	3(75)	**0.632**
7. Usual residence			
Rural	4(14)	1(25)	**0.512**
Urban	23(82)	3(75)	**0.584**
Foreigner	1(4)	0(0)	**0.875**

Women who had cervical dysplasia were all grouped as 'Abnormal' cervical cytology during the analysis. Fishers exact test was used to calculate this relationship as the expected number of abnormal cervical cytology was <5. There was a statistically significant association between being separated/divorced (p value 0.012) and the occurrence of abnormal cervical cytology. Nevertheless, there was no statistically significant association between cervical cytology (Normal/Abnormal) findings and participant's biological age, religion, level of education, occupation, rural/urban residency or socioeconomic status. Table 5 above describes this analysis.

3.5 Relationship between clinical characteristics and cervical cytological findings among renal transplant recipients.

Table 6: Clinical characteristics associated with cervical cytology findings among renal transplant recipients

		Cervical cytological abnormalities		
Factor		**Normal**	**Abnormal**	**P value**
		Frequency/ (Percent)	**Frequency/ (Percent)**	
Parity				
i)	0	6(21)	0(0)	**0.648**
ii)	1-3	15(54)	1(25)	**0.403**
iii)	4-6	7(25)	1(25)	**0.352**

Underlying cause of CKD				
i)	Hypertension	20(71)	3(75)	**0.689**
ii)	Diabetes	5(18)	0(0)	**0.488**
iii)	Polycystic Kidney disease	0(0)	0(0)	**0.875**
iv)	Chronic glomerulonephritis	1(4)	0(0)	**0.875**
v)	Infections	1(4)	1(0)	**0.238**
vi)	Connective tissue disorder	1(4)	1(25)	
Number of renal transplants				
1.	One	26(93)	3(75)	**0.340**
2.	>One	2(7)	1(25)	**0.340**
Immunosuppresive therapy				
i)	Cyclosporine +mycophenolate mofetil +steroid	11(38)	1(25)	**0.515**
ii)	Tacrolimus+ mycophenolate mofetil+steroid	9(34)	2(50)	**0.136**
iii)	Cyclosporine+ Azathioprine+ steroid	1(3)	1(25)	**0.875**
iv)	Tacrolimus+ Azathioprine+ Steroids	2(7)	0(0)	**0.762**
v)	Others	5(17)	0(0)	**0.488**
Age at first coitus				
i)	<14yrs	2(7)	0(0)	**0.762**
ii)	15-17yrs	4(14)	0(0)	**0.569**
iii)	18-21yrs	12(45)	1(25)	**0.597**
iv)	21-24yrs	8(28)	2(50)	**0.368**
v)	Cannot Remember	1(3)	1(25)	**0.875**
vi)	>24yrs	1(3)	0(0)	**0.875**

Number of lifetime sexual partners				
	i) Single	14(50)	4(100)	**0.085**
	ii) Multiple	14(50)	0(0)	**0.085**
Previous history of STI				
i)	Yes	1(3)	1(25)	**0.238**
ii)	No	27(97)	3(75)	**0.238**

There was no statistically significant association between the clinical characteristics and cervical cytological findings. Table 6 above describes the clinical characteristics associated with cervical cytological findings

3.6 Relationship between socio-demographic characteristics and HPV infection among renal transplant recipients in KNH

Table 7: Socio-demographic characteristics associated with HPV infection among renal transplant recipients in KNH

	HPV Infection		
Demographic characteristics	**Positive**	**Negative**	**p-value**
	Freq/ (Percent.)	**Freq./ (Percent)**	
Age (in years)			**0.637**
< 20	0	0(0)	
20 – 29	3(30)	4(18.2)	
30 – 39	4(40)	5(22.7)	
40 – 49	2(20)	3(13.6)	
>50	1(10)	10(45.5)	
Marital Status			**0.001**
Married	2(20)	18(82)	
Single	6(60)	2(9)	
Separated/ Divorce	2(20)	0(0)	
Widowed	0(0)	2(9)	
Religion			**0.149**
Catholic	0(0)	4(18)	
Protestant	10(100)	18(82)	
Level of Education			**0.588**
None	0(0)	0(0)	
Primary	0(0)	1(5)	

Secondary	2(20)	7(32)	
College/University	8(80)	14(64)	
Occupation			**0.829**
Self employed	1(10)	3(14)	
Formal	5(50)	7(32)	
Business	2(20)	7(32)	
Student	0(0)	1(5)	
Unemployed	2(20)	4(18)	
Socio-economic status			**0.984**
Low	2(20)	5(23)	
Middle	1(10)	2(9)	
High	7(70)	15(68)	
Usual residence			**0.642**
Rural	1(10)	4(18)	
Urban	9(90)	17(77)	
Foreigner	0(0)	1(5)	

The marital status of the participant in the study was more likely to affect the prevalence of positive or negative HPV infection result at a statistically significant level of (p=0.001).

Single, separated and divorced study participants had high prevalence of positive HPV infection at 80% compared to married patients consisting of 20%. Considerably, the frequency of married patients in the sample was high 63%. Table 7 above describes the relationship between socio-demographic characteristics and HPV infection.

3.6 Relationship between clinical characteristics and HPV infection among renal transplant recipients at KNH

Table 8: Clinical characteristics associated with HPV infection among female renal transplant recipients at KNH

Clinical characteristics	HPV Infection		p-value
	Positive	Negative	
	Freq./Percent	Freq./ Percent	
Parity			**0.014**
vi) 0	5(50)	2(9)	
vii) 1-3	5(50)	13(59)	
viii) 4-6	0(0)	7(32)	
ix) 7-8	0(0)	0(0)	
x) >8	0(0)	0(0)	
Underlying cause of CKD			**0.250**
i. Hypertension	8(80)	15(75)	
ii. Diabetes	0(0)	5(25)	
iii. Polycystic Kidney Disease	0(0)	0(0)	
iv. Chronic glomerulonephritis	1(10)	0(0)	
v. Infections	0(0)	1(5)	
vi. Connective tissue disorder	1(10)	1(5)	
Number of renal transplants			**0.935**
1. One	9(90)	20(91)	
2. >One	1(10)	2(9)	
Graft function (Creatinine Levels) µmol/L			**0.274**
50-60	0(0)	1 (5)	
61-70	0(0)	2(9)	
71-80	5 (50)	3(14)	
81-90	1(10)	7(32)	
91-100	2(20)	4(18)	
>100	2(20)	5(23)	
Immunosuppresive therapy			**0.473**

i)	Cyclosporine +mycophenolate mofetil +steroid	3(30)	9(41)	
ii)				
iii)	Tacrolimus+ Mycophenolate mofetil+ steroid	4(40)	8(36)	
iv)	Cyclosporine+ Azathioprine+ steroid	1(10)	0(0)	
v)	Tacrolimus+ Azathioprine+ Steroids	0(0)	2(9)	
vi)	Others	2(20)	3(14)	
Age at first coitus				**0.544**
i)	<14yrs	1(10)	2(9)	
ii)	15-17yrs	4(40)	3(14)	
iii)	18-21yrs	4(40)	10(45)	
iv)	21-24yrs	0(0)	6(27)	
v)	Cannot Remember	0(0)	0(0)	
vi)	>24yrs	1(10)	1(5)	
Number of lifetime sexual partners				**0.021**
i)	Single	3(30)	11(50)	
ii)	Multiple	7(70)	11(50)	
Previous history of STI				**0.555**
i)	Yes	1(10)	1(5)	
ii)	No	9(90)	21(950	

Parity among the participant in the study was found to affect the prevalence of positive or negative HPV infection result at a statistically significant level of (p=0.014). Similarly, the number of lifetime sexual partners the participant had in the study was more likely to affect the prevalence of positive or negative HPV infection result at a statistically significant level of (p=0.021).A woman who had multiple sexual partners was more likely to have positive HPV infection as evident from the 70% of the positive cases of the total positive HPV infections from the study. Table 8 above shows this analysis.

3.7 Relationship between cervical cytology and HPV infection among female renal transplant recipients

Table 9: Relationship between cervical cytology findings and HPV infection among female renal transplant recipients at KNH

	HPV Infection			
	Positive Freq./ (Percent)	**Negative** Freq./ (Percent)	**P value**	**Odds ratio**
Cervical Cytology				
Normal	7(70)	21(95)	**0.149**	**0.111**
Abnormal	3(30)	1(5)	**0.149**	**9.000**

Table 9 above shows that there was no statistical significance between occurrence of HPV infection and cervical dysplasia. However, those that were HPV positive were 9 times more likely to have an abnormal cervical cytology than those without HPV infection.

Figure 1: Association between abnormal/normal cervical cytology findings and HPV infection

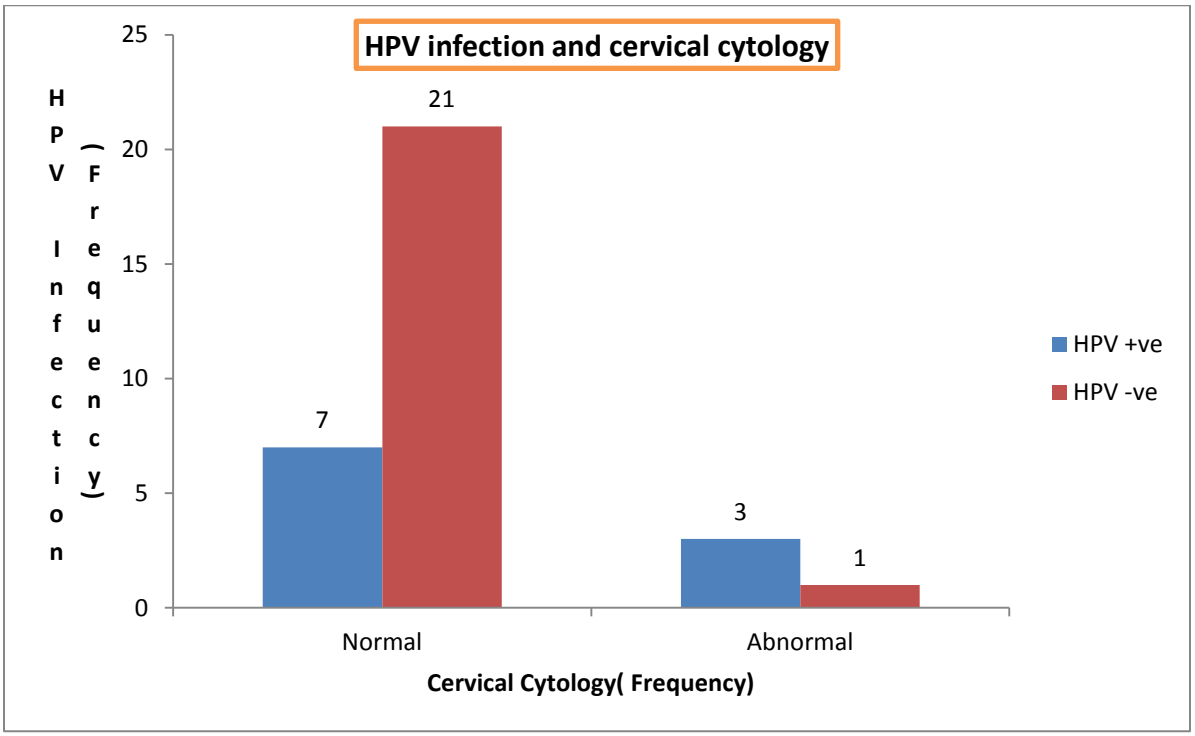


Figure 1 above, shows that 75% (3/4) of the study participants with abnormal cervical cytology were noted to be HPV positive. This indicates that patients with abnormal cervical cytology are more likely to have HPV infection.

CHAPTER 4

DISCUSSION

Cervical cancer accounts for 7.5% of all female cancers in less developed countries[37]. Among renal transplant recipients, the introduction of better immediate post-transplant care and use of multiple immunosuppressive therapies has resulted in longer life expectancies. One of the outcomes of this, is an upsurge of viral related malignancies, in this regard HPV related malignancies such as premalignant and malignant lesions of the cervix[24, 26]. Our study focused on assessing the prevalence of pre-malignant lesions of the cervix and HPV infection in this population, because though few in number, RTRs are at a higher risk than the general population and with proper screening guidelines, prevention and treatment of these lesions is possible.

Worldwide, the prevalence of hrHPV and abnormal cervical cytology among RTRs has been variable with some studies reporting very low and others high prevalence. Our study was cross sectional and we observed a prevalence of abnormal cervical cytology of 12.5% (4/32). This was higher than Morrison et al and Meuwiss et al who observed a prevalence of 0%(0/26) and 3.6% (8/224) respectively [38, 26]. This was however lower than the prevalence observed by Alloub et al of 53% (26/49) and comparable to Cordiner et al who observed a prevalence of CIN of 19.2% (5/26), who both did their studies prior to the introduction of use of combined immunosuppressant therapy for this population[39, 40]. These differences in prevalence may not only be attributed to the differences in the use of the newer versus the older combinations of immunosuppressant therapy, but also to the screening methods where some studies used both screening and diagnostic methods such as colposcopy, cervical cytology, and tissue biopsies while others used cervical cytology alone. Cordiner et al, found 2 cervical cytological abnormalities on pap smear and 3 others with normal cervical cytology were found to have CIN

on colposcopic biopsies. Conventional pap smear has a moderate sensitivity with observer differences and limitation in identification of small lesions, necessitating closer follow up and consideration of HPV detection methods with colposcopy for those found positive in this at risk population. Nevertheless, being a low resource setting, with colposcopies being few and the expertise being limited, annual pap smear still remains a good method of screening in this population.

The prevalence of hrHPV observed in our study was found to be at 31.3%. This is higher than what was reported by Morrison et al, Ghazizadeh et al, Pietrzak et al and Origoni et al who observed a prevalence of 5% (1/21), 6.9% (4/58), 18% (11/60) and 18.8% (9/48) respectively[38, 41, 24, 10]. Aggarwal et al in a study done in North India observed a prevalence of hr HPV comparable to our study of 32.5% (13/40)[42]. Our study was comparable to a study done in Mombasa, Kenya in the general population where the prevalence of hrHPV was 28.8%[43]. Nevertheless, like screening for cervical cytological abnormalities, the different methods of HPV DNA detection may be a factor in the varied differences of prevalence of HPV giving different sensitivities and specificities. Our study utilized the Cervista HPV HR test which uses the invader chemistry, a signal amplification method for detection of specific nucleic acid which is highly sensitive for hr HPV. Further to that, the high HPV prevalence in our study may be attributed to acquisition of new infections coupled with a lag in the clearance of these infections or as a result of reactivation of latent forms of HPV infection due to the immunosuppression.

The mean age in our study was 41.9 years, which was comparable to other studies assessing the prevalence of hrHPV infections among RTRs with mean ages ranging between 37 years and 43.9 years. HPV infections however tends to occur in younger populations. Hypertension and diabetes formed 87.5% of the cause for ESRD, both lifestyle diseases occurring in much older

populations. Moreover, those in a stable marital relationship were less likely to have HPV infection as compared to being single, divorced or widowed most likely due to their sexual behavior patterns such as concurrent sexual partners increasing STI acquisition as well as HPV.

As previously stipulated, sexual activity and behavior is the central risk factor in the causation of HPV infection and subsequent precancerous and cancerous lesions of the cervix. This encompasses early sexual debut, number of lifetime sexual partners, parity and history of STIs[9, 13]. In our study, we observed that the lifetime number of sexual partners was statistically significant (p value = 0.021) with more than 70% of those with hrHPV having multiple lifetime sexual partners. Both Halpert et al and Mayorgra et al also noted that the lifetime number of sexual partners was the single most independent risk factor which was unlike Morrison et al who further observed that recent sexual activity was a more important risk factor than past sexual behavior [28, 36, 38].Recent sexual behavior may plausibly explain the acquisition of new HPV infections. Of equal importance to the lifetime number of sexual partners in females, is the role of sexual behavior of the male counterparts regardless of their marital status, with concurrent sexual partners, polygamy and multiple sexual partners in the acquisition and spread of STIs as well as HPV infection and subsequent occurrence of premalignant lesions of the cervix. Our study however, did not look at this scope.

Long-term use of immunosuppressive therapy has been shown to increase the risk of occurrence of viral related pre-malignancies. The duration and drug dose combinations used are reported as important in the development of HPV infection. In our study, the mean duration of drug use was 4.89 years, majority (60%) of the women having being on treatment for less than 5 years and there was no statistical significance between the occurrence of cervical cytological abnormalities, HPV infection and the use of immunosuppressant therapy. This was equally observed by Origani

et al and Aggarwal et al whose study participants mean duration of drug use was 4.4 years and unlike Meuwiss et al, who observed a correlation between the use of immunosuppressive drugs and occurrence of cervical cytological abnormalities with a mean duration of immunosuppression of 7.3 years which was longer than all the above studies[10, 42, 26]. This further emphasizes the need for closer long term screening in the transplant population.

Due to the cross-sectional nature of this study, it lacked the power to determine and detect associations between socio-demographic, reproductive, clinical characteristics and occurrence of both cervical cytological abnormalities and HPV infection. It was also conducted at a single site with few women having undergone renal transplantation giving us a small sample size making generalizability of the study difficult. It may not be clear why fewer women with ESRD end up with renal transplants but this may be attributed to ESRD being lower in females than males and socio-cultural factors with potential donors being fewer for women than men. Nevertheless, in our study, we were able to use both pap smear and HPV DNA testing as cervical cancer screening methods. Moreover, despite the small numbers of female RTRs, KNH offered a good study site as it is a pioneer of renal transplantation in the public sector

With a prevalence of HPV infection of 31.3%, which is higher than that of the general population in Kenya of 9.1%[1], there is room for speculation on the role of HPV vaccination as primary prevention in the transplant population. However, a recent study done assessing the immunogenicity and safety of the quadrivalent HPV vaccine among transplanted individuals showed a suboptimal response[44]. Overall, the benefits of annual cervical cancer screening among female renal transplant recipients cannot be overemphasized, however, HPV testing may be done to determine those that may benefit from colposcopy as well as HPV vaccine.

CONCLUSION

The findings of this study confirm a high prevalence of not only HPV infection, but also for cervical dysplasia among the study population. Although it's not possible to confirm causal relationship between HPV infection and abnormal cervical cytology from this study, it does show a close association between the two. Our study further confirms that the single most independent risk factor to occurrence of HPV infection and premalignant lesions of the cervix is sexual activity; specifically marital status, parity and lifetime number of sexual partners are identified here as significant contributing factors.

RECOMMENDATIONS

i) KNH could form its own policies on the cervical cancer screening of transplant recipients and include it in the Standards of operating procedures of the post-transplant clinic this includes screening in the pre-transplant period. Further to this, the Ministry of Health may include these protocols in the screening for special populations in the "National Cervical Cancer Prevention Program' guidelines.

ii) Encourage uptake of cervical cancer screening services through health education on cervical cancer for the study population with primary prevention aiming at HPV vaccination and behavioural modification methods in order to reduce HPV exposure and secondary prevention aiming at early detection and treatment of cervical lesions. Thereby reducing the burden of disease that may occur as a result of multiple chronic diseases.

iii) There's a need for more longitudinal studies to assess the long term risk of immunosuppression in this population.

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APPENDIX I

PARTICIPANTS INFORMATION/CONSENT FORM

ENGLISH LANGUAGE VERSION

Project title**: PREVALENCE OF CERVICAL CYTOLOGICAL ABNORMALITIES AND HUMAN PAPILLOMA VIRUS INFECTION AMONG RENAL TRANSPLANT RECIPENTS**

INVESTIGATOR

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University of Nairobi

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The Chairperson, KNH –ERB

Prof. A.N. Guantai

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Telephone number: 2726360/27263600 Ext 44102

INTRODUCTION

My name is Dr. Millicent Masinde, I am a postgraduate student in the department of Obstetrics and Gynaecology at the University of Nairobi and I would like you to participate in this study. If you agree to join this study, you will be required to undergo a test called pap smear and liquid based cytology test. This shall then be taken to the University of Nairobi cytology laboratory and University of Manchester virology laboratory for processing and analysis. The purpose of this consent form is to give you the information you will need to help you decide whether to be in the study. Please read this form carefully. You may ask questions about what we will ask you to do, the risks, the benefits and your rights as a volunteer, or anything about the research or in this form that is not clear. When all your questions have been answered, you can decide if you want to be in this study or not. This process is called "informed consent".

Purpose and benefits

This study will help us to know how many of the participants will have abnormal cervical cytology among renal transplant women. Through this study we want to understand the burden of cervical cancer lesions in renal transplant recipients.

This study will benefit the society by providing information that can be used to improve services to ensure more renal transplant recipients are referred for cervical cancer screening services as part of their routine care at the post renal transplant clinic and even a push toward integration of these services.

At a personal level, participation in the study will provide an extra opportunity for women who did not know if they have precancerous or cancer lesions. Women identified as having abnormal results of the Pap smear will be referred to the hospital's colposcopy outpatient clinic for further follow up and management using routine referral system of the hospital.

Procedures

If you agree to participate in this study, you will be asked to fill a questionnaire which will look at aspects of your medical, social and sexual health.

After answering these questions, I, the researcher will proceed to do a pap smear. The procedure will involve, introduction of disposable speculum in your birth canal and then taking some cells from your cervix using a cytobrush to screen for Human papillomavirus(the virus that causes cancer of the cervix) and cervical abnormalities.

If the pap smear shows abnormal results, you will be referred to the gynaecology colposcopy clinic for further management and follow up.

The questionnaire shall be confidential and your number shall not be recorded in it. A serial number will be indicated for data analysis purposes. Your name shall not be used in any of the publications. This procedure will take 5 to 10 minutes.

The KNH Research and Ethics Board have given us permission to invite to participate in this study.

Risks, stress, or discomfort

I believe there is little risk of you participating in this study. A pap smear is not painful but may be a little discomfort or slight bleeding while taking the specimen. You may become embarrassed, worried, or anxious when answering some of the questions as they are of a personal nature but this will cause no harm. If this happens, we will slow down, take a break and if the procedure is too uncomfortable, we will withdraw altogether.

Compensation

There will be no costs to you for any of the activities in this study. There shall be no monetary gain on participating.

Voluntarism

Participation is free and voluntary. Your decision will not be used against you in anyway. If you choose to participate, you can change your mind at any point. This will not deter you from accessing any other services provided by the hospital.

Confidentiality

The information collected from this study will be kept private and confidential. Codes and not names shall be used to provide utmost privacy. The results of this study may be used in publications; however there shall be no information that will link the results to you.

Other information

If you have a problem that may be related to taking part in this research or any questions you can contact Dr. Millicent Masinde on 0721243740 and I will be glad to help where I can. If you have any questions about your rights as a research participant you may contact the chairperson of the Ethics Board on 2726300 ext. 44102.

Signatures for Consent

The above information describing the research, its benefits, risks and procedures has been read to me and explained. All my questions have been answered to my satisfaction.

I voluntarily agree to participate in this research study.

Name of patient _____Date_____

Signature or thumb print of patient_____

I certify that the nature and purpose, benefits and potential risks associated with participating in this research have been explained to the above volunteer.

Name of person obtaining Consent_____

Signature of the person obtaining consent ----------

Thank you for agreeing to participate in this research.

APPENDIX II/ KIAMBATANISHO II

IDHINI YA USHIRIKI KATIKA UTAFITI; MAKALA YA KISWAHILI

MAELEZO KWA MHUSIKA NA NAKALA YA KIBALI

UTAFITI: <u>UTAFITI YA KULINGANISHA KIWANGO CHA MAAMBUKIZI YA VIRUSI VYA BINADAMU VYA PAPILLOMA NA SARATANI YA NJIA YA KIZAZI BAINA YA WANAWAKE WALIOPANDIKIZWA FIGO.</u>

MTAFITI MKUU
Daktari Millicent Masinde
Idara ya Magonjwa ya Wanawake
Chuo Kikuu cha Nairobi
S.L.P. 19676-00202, Nairobi.
Simu ya mkono: 0721 243 740

Mwenye-Kiti Idara Ya Maswali Ya Utafiti:
Profesa A.N. Guantai
S.L.P. 20723-00202, Nairobi.
Simu: 2726360/ 2726300 Ext. 44102.

Kianzilishi

Habari? Jina langu ni Dkt. Millicent Masinde. Mimi ni mwanafunzikatika Idara ya magonjwa ya wanawakekatika Chuo Kikuu cha Nairobi. Ningependa kukualika kuhusika na utafiti huu. Ikiwa utakubali kuhusika, utahitajika kupimwakipimo cha saratani ya sehemu ya kizazi. Kipimo hiki kitatumwa katika mahabara ya Vyuo vikuu vya Nairobi na Manchester ilikufanyiwa uchunguzi. Maana ya hati hii ni kukuelezea juu ya utafiti huu. Tafadhili soma hati hii kwa maakini. Unaweza kuuliza maswali yoyote juu ya utafiti huu, madhara, manufaa na haki zako kama mhusika katika utafiti huu. Mchakato huu ni wito wa ridha.

Madhumuni na Manufaa ya Utafiti

Utafiti huu utatusaidia kujua ni wanawake wangapi waliopokea upandikizi wa figo wana maambukizi virusi vya binadamu papilloma na dalili ya saratani au saratani ya njia ya kizazi.

Utafiti huu utakuwa na faida kwa jamii kwa kutoa habari ambazo zinaweza kutumika katika kuboresha hudumakwawaliopandikizwafigo. Pia, kama huduma ya uchunguzi wa saratani inaweza kuwa na manufaa zaidi ikiwekwa katika kliniki baada ya kupandikiza figo na hata kushinikiza kuelekea ushirikiano wahuduma hizi.

Kwako binafsi, kwa kushiriki katika utafiti huu utapata nafasi ya kujua kama kuna dalili za saratani au saratani ya njia ya kizazi.Iwapo utapatikana na shida hii utaweza kutumwa katika kliniki ya colposcopy ilyo katika hospitali hii ambapo utatibiwa.
Utakapokubali kushiriki katika utafiti huu, utaombwa kujaza dodoso ambayo itaangalia masuala ya afyayako ya matibabu, kijamii na kijinsia.
Baada ya kujibu maswali haya,utalala katika kitanda kilicho kwenye chumba cha kupimwa na nitatumia speculum kuangalia njia yako ya uzazi. Kisha, nitatumia chombo cha cytobrush kuchukua seli kutoka mfuko wa uzazi wako. Hii ndiyo tutatumia kupima kama kuna dalili za saratani navirusi vya papilloma (virusi vinavyosababisha kansa ya uzazi). Kama kipimo hiki kitaonyesha matokeo yasiyokuwa ya kawaida, utatumwa katika kliniki ya magonjwa ya wanawake colposcopy kwaajili ya matibabu zaidi na kufuatilia.
Dodoso itakuwa siri na utapewa namba. Jina lako halitatumika popote. Taratibu hii itachukua dakika 5 hadi 10.
Utafiti KNH na Maadili Bodia imetupa ruhusa ya kukaribisha kushiriki katika utafiti huu.

Hatari, dhiki, au usumbufu

Naamini madhara yanayoweza kutendeka ni ya matokeo kidogo. ‘Pap Smear’sichungu lakini inaweza kuwa na usumbufu kidogo au kutokwa na damu kidogo wakati wa kuchukua sampuli. Unaweza kuwa na aibu au wasiwasi wakati wa kujibu baadhi ya maswali. Hali hii itakapotokea, tutapumzika kidogo. Ikiwa baada ya kupumzika kuna shida yoyote, tutawacha utaratibu huu.

Fidia

Hautakuwa na gharama kwa ajili ya shughuli yoyote katika utafiti huu. Pamoja na hayo, hautapata fedha kwa kushiriki.

Hiari

Ushiriki ni burena ya hiari. Unaweza kubadili akili yako katika hatua yoyote. Hii haitakuzuia kupata huduma zozote zingine zinazotolewa na hospitali.
Taarifa Nyingine
.

Siri

Taarifa zilizokusanywa kutoka utafiti huu utatunzwa binafsi na siri. Namba na wala si majina zitatumika kutoa siri mkubwa. Matokeo ya utafiti huu inaweza kutumika katika machapisho, hata hivyo hakutakuwa na habari itakayo weza kukuunganisha na matokeo.

Taarifa Nyingine

Kama unatatizo linalotokea kwasababu ya kuhusiana na kushiriki katika utafiti huu au maswali yoyote, unawea kuwasiliana na Dkt. Millicent Masinde kutumia nambari 0721243740. Kama una maswali yoyote kuhusu haki zako kama mshirika wa utafiti, unaweza kuwasiliana na mwenyekiti wa Bodi ya Maadili ukitumia nambari 020-276300 mwendelezo 44102

Saini kwa ajili ya Ridhaa

Nimeelezewa habari juu ya utafiti, faida zake,hatari na taratibu. Maswali yangu yote yamejibiwa na nimeridhika.
Nakubali kuhusika kwa huu utafiti kwa hiari bila kusurutishwa kwa njia yoyote.
Jina la Mhusika wa utafiti_____Tarehe_____

Sahihi au alama ya kidole gumba ya mhusika wa utafiti_____

Ninathibitisha kwamba nimemuelezea mhusika wautafiti asili na lengo, faida na uwezekano wa hatari zinazohusiana nakushiriki katika utafiti huu.

Jina la anayeomba utafiti_____Tarehe_____

Sahihi la anayeombautafiti_____

Asante sana kwa kukubali kushiriki katika utafiti huu.

APPENDIX III

Questionnaire

SOCIODEMOGRAPHIC CHARACTERISTICS

1. Study number [ ]

2. Age in years [ ]

3. Marital Status

1. Married 2. Single 3. Separated/ divorced 4. Widowed [ ]

4. Religion

1. Catholic 2. Protestant 3. Muslim 4. Others [ ]

5. Level of education

1. None 2. Primary 3. Secondary 4. College/University

5. No response [ ]

6. Occupation

1. Self employed 2. Formal employment 3. Business

4. Student 5. Unemployed [ ]

7. Socioeconomic status

1. Low(<KShs 10,000) 2. Medium(Kshs 10,001-25,000) 3. High (Kshs >25,000) [ ]

8. Usual residence

1. Rural 2. Urban 3. Foreigner [ ]

B. CLINICAL CHARACTERISTICS

9. Parity 1. Nulliparous

2. 1-3

3. 4-6

4. 7-8

5. >8 Specify……. [ ]

10. Age at menarche 1. Specify……..

2. Can't Remember [ ]

11. Age at first coitus

1. Before 14 years

2. 15-17 years

3. 18-21 years

4. 22-24 years

5. Not known but before menarche

6. Cannot remember

7. >24 years Specify…… [ ]

12. Number of sexual partners 1. Single

2. Multiple Specify……[ ]

13. Contraceptive use 1. Yes

2. No [ ]

Specify type……

14. Previous history of treatment of S.T.I? 1. Yes Specify……

2. No

3. Can't remember [ ]

Past medical history

15. Smoking status 1. Non-smoker 2. Previous smoker3. Current smoker [ ]

16. Age at onset of Chronic Kidney Disease 1. ……...

17. Duration of CKD 1. …….

18. Underlying cause of CKD

1. Hypertension 2. Diabetes 3. Polycystic Kidney Disease 4. Chronic glomerulonephritis 5. Infections 6. Others [ ]

19. Current Creatinine levels……..

20. Age at renal transplant . ……

21. Number of transplants 1 ONE

2. >ONE

22. Duration of years since renal transplant……

23. Any episodes of acute rejection that require dialysis

1. Once 2. More than once [ ]

24. Immunosuppresive treatment currently used

1. Cyclosporine+mycophenolate mofetil +steroid
2. Tacrolimus+mycophenolate mofetil+steroid
3. Cyclosporine+azathioprine+steroid
4. Tacrolimus+ Azathioprine+ Steroid
5. Others (Specify)……

25. Have you ever heard of a test called "pap smear"?

1. Yes 2. No [ ]

26. Do you know what it checks in the body? 1. Yes 2. No [ ]

If yes, what does it check? 1. Cancer of the cervix

2. Cancer of the uterus
3. Cancer
4. Can't remember [ ]

27. Have you ever done a pap smear? 1. Yes 2. No [ ]

a) If Yes how long ago……

b) Were you told the results 1. Yes 2. No [ ]

c) If Yes , what were the results 1. Normal

2. Abnormal [ ]

d) If Abnormal, did you receive treatment

1. Yes 2. No [ ]

Specify treatment received……..

28. Have you ever heard of Human papillomavirus

1. Yes 2. No [ ]

APPENDIX IV

CYTOLOGY REQUEST/REPORT FORM.

FILE No……..

RESEARCH No…….……..

AGE……..DATE……

CLINICAL OBSERVATION:

NORMAL INFLAMMED ERODED SUSPICIOUS

OTHERS SPECIFY……
…….

PROVISIONAL DIAGNOSIS…….

LAB REPORT

BETHSEDA CLASSFICATION

Suitability	Yes/No	ASCUS	☐
Adequacy	Yes/No	AGC	☐
Negative	☐	LSIL	☐
Inflammatory	☐	HSIL	☐
Reactive	☐	Glandular Neoplasia	☐

Comments……
……
……..……
……

Pathologist's Name……..Sign……..…

Lab Number……..Date..…….

APPENDIX V

REFERRAL FORM FOR PATIENTS WITH ABNORMAL PAP SMEAR

Name of the patient……..SEX……

AGE……

DATE…….

File number……..……..

Clinic referred from……..……

Clinic referred to…….

Results of the Pap Smear……...

……
…..

Reason for referral……..

Name of the referring Clinician……

Sign……..

APPENDIX VI: Formal request Letter for Material Transfer/ Shipment

31st March, 2014

HEAD,

DEPARTMENT OF STANDARDS AND REGULATORY SERVICES,

MINISTRY OF HEALTH,

AFYA HOUSE,

NAIROBI.

Dear Sir/Madam,

RE: REQUESTING SHIPMENT OF SPECIMEN SAMPLES TO MANCHESTER, U.K.

We kindly request that you consider our request to ship 50 samples of liquid based cytology smears from women in the study project " Prevalence of cervical cytological abnormalities and Human papillomavirus infection among renal transplant recipients at Kenyatta National Hospital" . These samples are to be shipped to the gynaecological Oncology laboratories, University of Manchester, U.K .

HPV genotyping and DNA viral load will be performed on all the patients recruited to evaluate the HPV genotype spectrum in the study population.

The Principal Investigator in this study is Dr. Millicent Masinde under the supervision of Dr. Eunice Cheserem, Dr. Wanyoike Gichuhi and Prof. Joshua Kayima as part fulfillment of Masters of Medicine in Obstetrics and Gynaecology. The KNH-ERC study approval number is_____.

The samples will be shipped to the laboratory at the following address:

Dr. Ian Hampson,

Head, Gynaecological Oncology Labaratories,

Department of Gynaecological Oncology,

University of Manchester,

Oncology Laboratory, Room 100,

St. Mary's Hospital, Oxford Road,

Manchester M13, 9WL, UK.

Attached is a copy of the KNH-ERC approval letter and the Study Proposal submitted to KNH-ERC. Thank you for your assistance.

Yours faithfully,

Dr. Millicent Masinde.

APPENDIX VII

PROJECT BUDGET

NO	ITEM	QUANTITY	UNIT PRICE	TOTAL
A	**LABORATORY**			
1.	Pap kits	35	600	21,000
2.	Disposable speculum	35	100	3,500
3.	Gloves in pairs	100	50	5,000
4.	Thin prep bottles	50	-	-
5.	Pathologist fees	32 Samples	500	16,000
6.	Transport of specimens to Manchester	32 Samples	-	20,000
B.	**Statistician fee**	1	20,000	20,000
C.	**Stationary/Printing**			
1.	Questionnaire+ consent forms	50x7pages	10	3,500
2.	Pens	6	50	300
3.	Notebooks	2	150	300
4.	Final manuscript	4	1000	4000
D.	**GRAND TOTAL**			**KSHS 92,600**

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KNH/UON-ERC
Email: uonknh_erc@uonbi.ac.ke
Website: www.uonbi.ac.ke

KENYATTA NATIONAL HOSPITAL
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Ref: KNH-ERC/A/220 Link:www.uonbi.ac.ke/activities/KNHUoN 4th July 2014

Dr. Millicent Spensa Masinde
Dept.of Obs/Gynae
School of Medicine
University of Nairobi

Dear Dr. Masinde

Research proposal: Prevalence of cervical cytological abnormalities and Human Papilloma virus Infection among Renal transplant recipients at Kenyatta National Hospital (P192/04/2014)

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and approved your above proposal. The approval periods are 4th July 2014 to 3rd July 2015.

This approval is subject to compliance with the following requirements:

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

For more details consult the KNH/UoN ERC website **www.uonbi.ac.ke/activities/KNHUoN.**

Yours sincerely

PROF. M. L. CHINDIA
SECRETARY, KNH/UON-ERC

c.c. The Principal, College of Health Sciences, UoN
The Deputy Director CS, KNH
The Chairperson, KNH/UoN-ERC
The Assistant Director, Health Information, KNH
The Dean, School of Medicine,UoN
The Chairman, Dept.of Obs/Gynae, UoN
Supervisors: Dr. Eunice Cheserem,Dr.J.Wanyoike,Gichuhi, Prof.Joshua K Kayima

MINISTRY OF HEALTH
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MOH/ADM/1/81/VOL.1

17th July, 2014

Dr. Millicent Masinde
University of Nairobi
College of Health Sciences
P.O. Box 19676 – 00200
NAIROBI

Dear Dr. Masinde

RE: AUTHORITY TO SHIP BIOLOGICAL SAMPLES

Your request for specimen export permit dated 8th July, 2014 refers.

Te title of the study is noted to be *"Prevalence of cervical cytological abnormalities and Human Papilloma virus Infection among Renal transplant recipients at Kenyatta National Hospital (192/04/2014)".*

Authority is hereby granted for shipment of biological samples related to this research work:

- 50 samples of liquid based cytology smears.

The shipment contact details are follows:

Dr. Ian Hampson,
Head, Gynaecological Oncology Labaratories,
Department of Gynaecological Oncology,
University of Manchester,
Oncology Laboratory, Room 100,
ST. Mary's Hospital, Oxford Road,
Manchester M13, 9WL, UK.

17/7/14

Dr. Onyancha P. K.
FOR: DIRECTOR OF MEDICAL SERVICES

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Ref: KNH-ERC/SH/67

27th November 2014

Dr. Millicent Spensa Masinde
Dept.of Obs/Gynae
School of Medicine
University of Nairobi

Dear Dr. Masinde

Re: Approval for shipment of samples 'Prevalence of cervical cytological abnormalities and human papilloma virus infection among renal transplant recipients at Kenyatta National Hospital' (P192/4/2014)

Refer to your communication of 3rd November 2014.

The KNH/UoN-ERC has reviewed and approved shipment of 32 samples of liquid based cytology smears to the University of Manchester, UK for further analysis.

The samples will be under the custodian of:

Dr. Ian Hampton
Head, Gynaecological Oncology Laboratories
Department of Gynecological Oncology
University of Manchester
Oncology Laboratory, Room 100
St Mary's Hospital, Oxford Road
Manchester M13, 9WL, UK

Yours sincerely

PROF. M.L. CHINDIA
SECRETARY , KNH/UON-ERC

c.c. The Principal, College of Health Sciences, UoN
The Deputy Director, CS, KNH
The Chair, KNH/UoN-ERC
The Dean, School of Medicine,UoN
The Chairman, Dept.of Obs/Gynae, UoN
Supervisors: Dr.E. Cheserem,Dr.J. Wanyoike Gichuhi,Prof.Joshua K Kayima