BURDEN OF CANCER ASSOCIATED WITH INFECTIOUS AGENTS AT TWO REFERRAL HOSPITALS, KENYA

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DECLARATION

This dissertation is my original work and has not been presented for the award of a degree in any other university.

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DEDICATION

This work is dedicated to my parents Dr. Charles M. Wanjigi and Sarah N. Macharia whose love and support has been my strength all through. You are the best gift God ever gave to me.

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LIST OF ABBREVIATIONS

AIDS	-	Acquired immune deficiency syndrome
AMPATH	-	Academic Model Providing Access to Healthcare
ATL	-	Adult T-cell Leukemia
CD4	-	Cluster of Differentiation 4
CDC	-	Centers for Disease Control
CLD	-	Chronic liver disease
CMV	-	Cytomegalovirus
EBV	-	Epstein Barr Virus
ESCC	-	Esophageal squamous cell carcinomas
H.PYLORI	-	*Helicobacter pylori*
HAART	-	Highly Active Antiretroviral Therapy
HBV	-	Hepatitis B virus
HCC	-	Hepatocellular carcinoma
HCV	-	Hepatitis C virus
HHV-8	-	Human Herpes Virus 8
HIV	-	Human Immunodeficiency Virus
HL	-	Hodgkin Lymphoma
HPV	-	Human papilloma virus
HTLV	-	Human T-cell leukemia virus
IARC	-	International Agency for Research on Cancer
KS	-	Kaposi Sarcoma
NCD	-	Noncommunicable disease
NCI	-	National Cancer Institute
NHL	-	Non Hodgkin Lymphoma
SPSS	-	Statistical Package for Social Sciences
SV 40	-	Simian Virus 40
WHO	-	World Health Organization
XMRV	-	Xenotropic Murine Leukemia Virus-Related virus

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Abstract

Background: Infectious agents accounts for nearly 18% of the global cancer burden, with higher percentages in developing countries. The commonest infectious agents associated with cancer morbidity worldwide include, *Helicobacter pylori* (*H. pylori*) which accounts for 5.5%, Human papilloma virus (HPV) which accounts for 5.2% of all cancers, Hepatitis B and hepatitis C viruses which account for 4.9% of all cancers, Epstein Barr virus, Kaposi's sarcoma associated herpes virus, human T-lymphotropic virus 1(HTLV-1) and Human Immunodeficiency Virus.

Objective: To determine the burden of cancer at Kenyatta National Hospital and Moi Teaching and Referral Hospital

Study method:

This study was a cross-sectional health facility-based retrospective survey conducted at Kenyatta National Hospital and Moi Teaching and Referral Hospital for the time period 2008 to 2012.

Data was obtained from the patient's files from the medical records department of the selected hospitals. A pre-designed data collection form was used to collect data from patient's files which met the inclusion criteria. Demographic information and cancer data was extracted in relation to age and sex. The study was approved by the KNH/U.o.N Ethics and Research Committee.

Results:

A total of 500 files were sampled randomly in KNH and MTRH from 2008 to 2012. In KNH 60% were females and 40% were males. The age ranged from 18 to 95years with a mean of 51years. Patients between the ages of 35 years to 74 years were 76.4% with the highest age group (55-64 years) with 22.8%. In females (n=300) the five most common cancers were cervical 62(20.7%), breast 59(19.7%), leukemia 25(8.3%), ovary 22(7.3%) and gastric 15(5%). In males (n=200) the five most common types of cancers were prostate 23(11.5%), laryngeal 19(9.5%), colorectal 17(8.5%), leukemia 16(8.0%) and esophageal 14(7.0%). The five prevalent

cancers associated with infectious agents in both sexes, were cervical (12.4%), gastric (5.4%), Prostate (4.6%), nasopharyngeal carcinoma (3.4%), Non Hodgkin's Lymphoma (2.6%) and liver cancer (2.0%). In MTRH, 56% of the cases were females and 44% were males. Mean age was 48 years (18years to 90 years). A majority of patients (76.6%) were between 25 to 64 years. Those aged 35 to 44 years had the highest percentage (22.8%). In females (n=300) the five most common cancers were cervical 62(20.7%), breast 59(19.7%), leukemia 25(8.3%), ovary 22(7.3%) and gastric 15(5%). In males (n=200) the five most common types of cancers were prostate 23(11.5%), laryngeal 19(9.5%), colorectal 17(8.5%), leukemia 16(8.0%) and esophageal 14(7.0%). The five prevalent cancers associated with infectious agents in both sexes were: Kaposi's sarcoma (18.6%), Cervical (8.6%), Non-Hodgkin's Lymphoma (7.4%), Liver (3.2%) and Gastric (3.0%).

Conclusion

This study provided data on common types and prevalence's of cancer and demonstrated that cancers associated with infectious agents contribute to the high burden of cancer in Kenya although causation was not proven. Strategies to increase the use of preventive measures such as increased awareness, vaccination, early and regular screening and treatment should be enforced in the context of limited resources as majority of these cancers can be prevented.

Keywords: cancer, infectious agents, Sub-Saharan Africa, Kenya

CHAPTER 1: BACKGROUND

In Africa, cancer is an emerging public health problem where about 715,000 new cancer cases and 542,000 cancer deaths occurred in 2008 according to the International Agency for Research on Cancer (IARC)(Ferlay et al., 2010). According to the United Nation's population estimates, the African population is projected to increase by 50% overall, from 1.03 billion to 1.52 billion between the years 2010 and 2030. Specifically, it is projected to increase by 90% for those aged 60 years and above, the age at which cancer most frequently occurs. Although this is likely to be accompanied by increased burden of cancer, the disease continues to receive low public health priority in Africa, largely because of limited resources and other pressing public health problems, including communicable diseases such as HIV/AIDs, malaria, and tuberculosis(ACS, 2011, Jemal et al., 2011). In Eastern Africa, Cervical cancer was the leading cause of cancer death in women in 2008 while Kaposi sarcoma was the commonly diagnosed cancer and the leading cause of cancer death among men (Globocan, 2008).

Nearly 18% of the global Cancer burden is attributable to infectious agents, with a higher percentage (26.3%) in developing countries than in developed countries (7.7%) (Parkin, 2006, Mackay et al., 2006). According to the World Health Organization, about 20% of all cancer cases worldwide are related to chronic infections where up to 15% of them have a viral etiology with higher incidence in developing countries than in the rest of the world. These are viruses such as Human Papilloma Virus (HPV), which accounts for 5.2% of all cancers (de Martel et al., 2012). According to World Cancer report (2008), infections are thought to be responsible for 85% of all hepatocellular carcinomas with Hepatitis B virus (HBV) and Hepatitis C virus (HCV) accounting for 54.4% and 31.0% of them, respectively.

Other virus associated cancers include: Kaposi's sarcoma (caused by human herpesvirus 8), adult T-cell leukemia (caused by human T-cell leukemia virus type 1) and lymphomas caused by Epstein Barr virus (de Martel et al., 2012, Parkin, 2006).

Helicobacter pylori is a bacteria associated with cancer, accounting for 5.5% of all cancers. For example, between 74% and 78% of all stomach cancers worldwide have been attributed to infections with H. pylori *(Parkin, 2006).* In addition, other microorganisms, including parasites such as *Schistosoma haematobium* and *Opisthorchis viverrini* may also be involved, acting as cofactors and/or carcinogens (Oluwasola AO, 2005, Parkin, 2006).

The occurrence of cancer in Africa varies due to differences in exposures to major risk factors, detection practices that include diagnostic and screening services, awareness of early signs and symptoms and availability of treatment. Although cancers related to infectious agents are among the dominant types in developing countries, cancers dominating some developed countries are becoming more common also in these countries due the adoption of unhealthy lifestyles.

Comprehensive data on the burden of cancer associated with infectious agents are needed to inform policies, strategies and interventions are lacking in most countries in eastern African region particularly Kenya.

CHAPTER 2: LITERATURE REVIEW

2.1. INTRODUCTION

Cancer is a term used to describe a group of malignant tumors with a common characteristic of uncontrolled growth of abnormal cells that have acquired the capability to spread and metastasize to distant site through the circulation. Cancer is of multifactorial etiology involving interplay between genetic and environmental factors, including infectious agents, ultimately leading to a cascade of genotypic and phenotypic changes that culminates in the formation of a malignant tumor (Oluwasola et al., 2005).

Cancer is the leading cause of death in developed countries and the second leading cause of death in developing countries (Table 5). This demographic shift of cancer burden in developing countries is compounded by increasing population growth and aging, entrenchment of modifiable risk factors such as smoking, physical inactivity, unhealthy diets, reproductive behaviors, HIV-associated cancers and by the slower decline in cancers of infectious etiologies.

2.2. CANCERS ASSOCIATED WITH INFECTIOUS AGENTS

2.2.1. Gastric cancer and *H. pylori*

H.pylori is a spiral, gram-negative bacterium that colonizes the stomach whose most probable route of transmission is through fecal oral or oral-oral routes. Contaminated water sources could act as reservoirs. Worldwide, 75% of people are infected, with prevalence being higher in sub-Saharan Africa, where it is associated with 63.4% of all stomach cancers (Parkin, 2006). *H.pylori* is believed to induce chronic inflammation, which can lead to atrophic gastritis and, over time, increases the risk of developing gastric adenocarcinoma and gastric lymphoma (Plummer et al., 2004). In developing countries, the age at onset of infection is generally lower and peaks at 90 % among young adults (Plummer et al., 2004). Eating diets rich in smoked foods, salted meat or fish, pickled vegetables and smoking increases the risk factors for stomach cancer (ACS, 2011)

2.2.2. Cervical cancer and Human papilloma virus (HPV)

According to the world cancer report 2008, about 80% of cervical cancer cases occur in developing countries where, in many regions, it is the most common cancer among women**.** HPV 16 and HPV 18 have the highest prevalence among cervical cancer patients (50.5 and 13.1%, respectively) and are associated with a 200-fold increased risk of cervical cancer (Munoz et al., 2003).The cancer-causing strains of HPV are known to disrupt the cell cycle and inactivate tumor suppressor proteins such as p53, which enables genetic damage to accumulate and, eventually, a cancer to form (Tommasino et al., 2003).The cumulative lifetime probability of acquiring a cervical infection with at least one type of HPV is extremely high for sexually active individuals but most infections disappear spontaneously within 2–4 years, and only a small percentage progress to low- and high-grade squamous intraepithelial lesions influenced by,

smoking, increasing parity (number of children) and co-infection with herpes simplex virus or Chlamydia (ACS, 2011).

2.2.3. Liver cancer

2.2.3.1 Hepatitis B virus (HBV)

Approximately 54% of liver cancer worldwide is attributed to chronic infection with HBV (Parkin, 2006). To fight off the infection, the immune system releases cytokines and other inflammatory proteins that can cause tissue damage. Over time this can lead to cirrhosis of the liver, which is a strong predisposing factor for liver cancer (Azam and Koulaouzidis, 2008).

Chronic infection is indicated by persistence of hepatitis B surface antigen in the blood after the acute infection has passed. Chronicity is much higher for infants and children than for adults. HBV may be transmitted by mucous membrane or skin contact only when there are breaks, by injection or sexual intercourse, from a mother to her baby during birth, from sharing of toothbrushes and cutting items. Health care workers and patients with exposure to pooled blood products, such as hemophiliacs, are also at increased risk of exposure (Nelson et al., 2001).

2.2.3.2. Hepatitis C virus (HCV)

HCV infection affects more than 170 million individuals worldwide and represents one of the main causes of chronic liver disease (CLD) that can evolve in hepatocellular carcinoma (HCC) (Balsano and Alisi, 2007). A person infected with HCV has over 80% probability of becoming a chronic carrier. Direct transmission by blood contamination is the most important mode of HCV transmission. Chronic inflammation and cirrhosis are believed to play key roles in promoting HCV-associated HCC, although the underlying mechanisms of this process are not yet understood. In addition to HCC, HCV is also involved in polyclonal B lymphocyte activation

(Ferri et al., 2007). Cofactors that may influence progression are alcohol intake, age at infection and co infection with HBV or HIV (Flamm, 2003).

2.2.4. Epstein Barr virus (EBV) associated cancers

This virus belongs to Herpesviridae family and can establish long-term viral infection in their target cells, promoting cellular immortalization and transformation (Damania 2007). EBV is transmitted primarily via saliva and during adolescence or young childhood; it is associated with infectious mononucleosis. EBV has been implicated in the occurrence of nasopharyngeal carcinoma, in the pathogenesis of Burkitt's lymphoma and Hodgkin's disease (Cohen et al., 2008). EBV is also associated with some AIDS-related Non Hodgkin Lymphoma (NHL) and Hodgkin Lymphoma (Sasco et al., 2010).

2.2.5. Adult T-cell Leukemia & Human T-lymphotropic virus 1(HTLV-1)

HTLV-1 is an oncogenic virus associated with Adult T-cell Leukemia (ATL) which is an aggressive clonal malignancy of mature CD4+ T lymphocytes that presents after a 20-40 years of clinical latency (Yasunaga and Matsuoka, 2007). HTLV-1 still represents the only known human retrovirus directly linked to a specific human malignancy and is implicated as the aetiologic agent of ATL in that its patients are always found with the virus (Bergonzini et al., 2010).

2.2.6. Bladder cancer and *Schistosoma haematobium*

Chronic infection with *Schistosoma haematobium* in developing countries accounts for about 50% of the total bladder cancer burden, particularly in Africa and the Middle East (Parkin, 2006). Squamous cell carcinoma is the cancer associated with schistosomiasis (Parkin et al., 2006; Mostafa et al., 1999). Schistosoma infection to human is through direct skin penetration by aquatic cercariae. The parasite then migrates into circulation, matures and lodges in the venous plexus of the bladder where male and female adults mate to produce eggs. The eggs are laid in

the bladder, upper urinary and genital tract and the immune responses to these eggs results in an inflammation that leads to carcinogenesis (Fu et al., 2012).

2.2.7. Prostate cancer and infectious agents

Prostate cancer is the most commonly diagnosed cancer among men in Southern Africa and Western Africa (Jemal et al., 2011). Reports have shown various viruses (Urisman et al., 2006, Zambrano et al., 2002) and bacteria (Dennis et al., 2002) that are associated with prostate cancer. These infectious agents may contribute to chronic inflammation of the prostate and Tumorigenesis (De Marzo et al., 2007). Xenotropic Murine leukemia virus-related virus (XMRV) is a γ retrovirus that has been associated with prostate cancer (Urisman et al., 2006). XMRV is a candidate human tumor virus with a reduced activity variant of the antiviral gene, *RNASEL* which is the hereditary prostate cancer 1 gene or *HPC1* (Urisman et al., 2006) it is a member of a viral family known to cause leukemias and lymphomas in different mammalian species (Goff et al., 2007). XMRV integration sites in human prostate cancer tissues were mapped to cancer breakpoints, common fragile sites, micro-RNA genes, and cancer-related genes (Kim et al., 2008). Many of these genes are implicated directly or indirectly in prostate cancer and metabolic pathways that affect prostate cancer, including androgen signaling. XMRV has also been observed in prostate tissue from a nonfamilial prostate cancer patient and in an individual without prostate cancer (Fischer et al., 2008). Bacteria that can infect the human prostate primarily include *Escherichia coli* and *Enterococcu*s species (Brede and Shoskes, 2011). Connections between persistent mycoplasma infection and induced transformation of cultured cells, mycoplasmas have been postulated to play a role in human carcinogenesis (Sfanos and Isaacs, 2011). The adult of *S. haematobium* tend to deposit their eggs in the wall of the urinary bladder and to a lesser extent in the uterus, vaginal wall and prostate gland and infections with

these large numbers of schistosome eggs at a young age could be one of the causal factors for development of cancer (Fu et al., 2012).

2.2.8 Kaposi sarcoma and Human herpes virus 8 (HHV-8)

HHV-8 is a member of the Herpesviridae family that can establish long-term viral infections in their target cells promoting cellular immortalization and transformation (Elgui de Oliveira, 2007). KS is an endemic tumor of the Mediterranean basin and Africa (Ganem, 2010) rarely life threatening but usually affects elderly males with skin localization. KS has been recognized associated with HIV infection and therefore classified as AIDS defining disease (Sasco et al., 2010). In AIDS patients, KS displays frequent involvement of extra-cutaneous sites, typically lungs and gastrointestinal tract with complications (Bergonzini et al., 2010).

2.3. OTHER SELECTED CANCERS

2.3.1. Breast cancer

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death in females worldwide (Globocan 2008), its risk increases with inheritance of cancer susceptibility genes BRCA1 and BRCA2 (Chen and Parmigiani, 2007), age, family history of breast cancer, high breast tissue density (Boyd et al., 2007), breast tissue confirmed biopsy hyperplasia and high-dose radiation to the chest as a result of medical procedures (Ma et al., 2008). Other factors that increases the risk include never having children, a long menstrual history, recent use of oral contraceptives, and having first child after the age of 30 (Hulka and Moorman, 2008). Some potentially modifiable risk factors include being overweight after menopause, use of menopausal hormone therapy (especially combined estrogen and progestin therapy), physical inactivity and heavy alcohol consumption. Numerous studies have also shown that EBV (Mazouni et al., 2011,

Yasui et al., 2001), HPV (Wang et al., 2012) and cytomegalovirus (CMV) infections are associated with the development of breast cancer (Richardson et al., 2004).

2.3.2. Colorectal cancer

Colorectal cancer is the fourth most commonly diagnosed cancer in males and females in developing countries, with over 0.5 million new cancer cases and 288,500 deaths estimated to have occurred in 2008 (Table 6). Its risk increases with age, inherited genetic mutations (like Lynch syndrome and familial adenomatous polyposis), a history of colorectal cancer and/or polyps, or a history of chronic inflammatory bowel disease. Modifiable factors associated with increased risk of colorectal cancer are obesity, physical inactivity, a diet high in red or processed meat, heavy alcohol consumption, and smoking (ACS, 2011).

2.3.3. Lung and Bronchus cancer

Cigarette smoking is the most important risk factor for lung cancer, accounting for about 80% of lung cancer cases in men and 50% in women worldwide (Mackay et al., 2006). Other risk factors include secondhand smoke, occupational or environmental exposures to radon and asbestos, certain metals (chromium, cadmium, and arsenic), some organic chemicals, radiation, air pollution, coal smoke, and indoor emissions from fuels. Genetic susceptibility contributes to risk, especially in those who develop the disease at a younger age (Li and Hemminki, 2004).

2.3.4. Esophageal cancer

Esophageal cancer is almost twice common among men than women (Table 6). Cancer of the esophagus usually occurs as either squamous cell carcinoma in the middle or upper third of the esophagus, or as adenocarcinoma in the lower third or junction of the esophagus and stomach. The greatest risk factors for squamous cell esophageal cancer are heavy drinking and smoking while those of adenocarcinoma of the esophagus are smoking and low fruit and vegetable

consumption; however, the main risk factors are thought to be overweight and obesity and chronic gastro esophageal reflux disease when stomach contents enter the lower section of the esophagus irritates it and over time, can lead to Barrett's esophagus, a condition in which the cells lining the lower part of the esophagus have changed or been replaced with abnormal cells that could lead to cancer of the esophagus (ACS, 2011).

2.3.5. Non-Hodgkin's lymphoma (NHL)

The incidence of NHL in some parts of sub-Saharan areas particularly in East Africa, is influenced by the high incidence of Burkitt's lymphoma (a subtype of NHL) among children. This increase may be in part due to the AIDS epidemic (Parkin et al., 2010, Sriplung and Parkin, 2004). The risk for NHL is elevated in persons with organ transplants who receive immune suppressants to prevent transplant rejection, in people with severe autoimmune conditions, and in people infected with HIV, human T-cell leukemia virus type I (HTLV-I), and probably HCV (Hartge et al., 2006). NHL is classified as an AIDS-defining illness and is more prevalent among AIDS patients compared to the general population (Sasco et al., 2010). Epstein-Barr virus causes Burkitt's lymphoma and may play a role in other subtypes of NHLs. A family history of lymphoma and certain common genetic variations in immune response genes are associated with a modestly increased risk. Occupational exposures to herbicides, chlorinated organic compounds, and certain other chemicals are also associated with moderately increased risk (Hartge et al., 2006).

2.3.6. Cancers of the Lip and Oral cavity

Smoking, alcohol use, smokeless tobacco products, and HPV infections are the major risk factors for oral cavity cancer, with smoking and alcohol having synergistic effects (Hashibe et al., 2009). Worldwide, smoking accounts for 42% of deaths from cancers of the oral cavity (including the pharynx) and heavy alcohol consumption for 16% of the deaths (Danaei et al., 2005).

2.4. KENYAN SITUATION

Cancer in Kenya ranks third as a cause of death after infectious and cardiovascular diseases. Although population based data in Kenya does not exist cancer is estimated to cause 7% of total national mortality every year. The most common cancers in women are breast, esophagus and cervical cancer while in men it is esophagus, prostate cancer and Kaposi sarcoma. The rapid rise in cancers has resulted from increased exposure to risk factors which include tobacco, alcohol and exposure to environmental carcinogens. Other risk factors include infectious diseases resulting from viral, bacterial and parasitic infestations. Despite the fact that cancer is on the increase, the health systems in the country have traditionally concentrated on the prevention and control of communicable diseases (MOPHSMOMS, 2012).

According to the situation analysis of cancer in Kenya 2011(PB, 2011), the major policy concern however is that the Government of Kenya (Ministry of Public Health and Sanitation) has never had any designated programme or budget line for addressing cancer among other non communicable diseases that are silent killers. The Kenya Cancer Association claims that the government has continually neglected allocating sufficient funds for treatment of cancer patients. It's directing all its efforts on combating HIV/AIDS and that one-third of Cancer deaths could be avoided through Prevention and another third through early Detection and Treatment (KenCASA, 2011).

Cancer now poses a burden to the country which unless it is addressed will over whelm the country in the near future. Available cancer data is wanting, as there is currently no national cancer registry. Majority of cancer cases are diagnosed at advanced stages, when very little can be achieved in terms of curative treatment. This is largely due to the low awareness of cancer signs and symptoms, inadequate screening services, inadequate diagnostic facilities and poorly structured referral facilities. According to the situation analysis of cancer in Kenya 2011, the country has few cancer specialists who are concentrated in a few health facilities in Nairobi. Kenyatta National Hospital, the only Public institution that hosts most of the Cancer Experts and Technology in Kenya, is currently overwhelmed with Inpatient and Outpatient Cases and simply cannot cope. This makes it difficult for a great majority of the population to access cancer treatment services resulting in long waiting times causing some previously curable tumors to progress to incurable stages. According to the Cancer Association the devolution of cancer treating facilities at country level is necessary (KenCASA, 2011).

There are more Cancer cases being reported in Kenya now than years ago, but studies to determine the reasons for the increased prevalence and incidence are not being conducted. Cancer research is an essential element in the effective prevention and control of cancer (MOPHSMOMS, 2012).

CHAPTER 3: RESEARCH DEFINITION

3.1 JUSTIFICATION

Cancer is a major non-communicable disease (NCD) and noncommunicable diseases are estimated to account for over 60% of total mortality every year and 28% of all deaths in Kenya. Cancer in Kenya ranks third as a cause of death after infectious and cardiovascular diseases. Although population based data in Kenya does not exist it is estimated that the annual incidence of cancer is about 28,000 cases and the annual mortality is 22,000 (MOPHSMOMS, 2012).

The African population is projected to increase by 50% overall, between the years 2010 and 2030. Specifically, it is projected to increase by 90% for those aged 60 years and above, the age at which cancer most frequently occurs (ACS, 2011). Data from the CIA World Fact Book 2013 shows that, the life expectancy in Kenya is about 61.8 years for males and 64.8 years for females and this increased life expectancy reflects an increased risk for cancer acquisition (CIA, 2013).

Available cancer data is wanting as there is currently no national cancer registry in Kenya. It is estimated that more than half of all cancer cases and deaths worldwide are potentially preventable especially those associated with infectious agents if only given the required public health priority (ACS, 2011). This study aims to provide data on common types and trends of cancer especially that associated with infectious agents. This information will ultimately assist in formulating and implementing policies, focus on prevention, treatment, and control interventions in the context of limited resources.

3.2. RESEARCH QUESTION

What is the burden of cancer associated with infectious agents at Kenyatta National Hospital and Moi Teaching and Referral Hospital in Kenya?

3.4. OBJECTIVES

3.4.1. General objective

To establish the burden of cancer associated with infectious agents at two referral hospitals in Kenya from 2008 to 2012.

3.4.2. Specific objectives

1. To determine the types of cancer at Kenyatta National Hospital and Moi Teaching and Referral Hospital from 2008 to 2012.
2. To determine the trends of cancer at Kenyatta National Hospital and Moi Teaching and Referral Hospital from 2008 to 2012.
3. To determine the types and trends of cancer associated with infectious agents at Kenyatta National Hospital and Moi Teaching and Referral Hospital from 2008 to 2012.

CHAPTER 4: RESEARCH METHODOLOGY

4.1. Study sites

The study was conducted at two Referral Hospitals in Kenya namely: Kenyatta National hospital (KNH) and Moi Teaching and Referral Hospital (MTRH). The above facilities were selected because they are national hospitals and they host large numbers of patients.

4.2. Study design

The study was a cross sectional descriptive study.

4.3. Study population

Data was collected from hospital records of patients aged 18 years and above.

Inclusion criteria

- Hospital records of patients diagnosed with cancer during the period 2008 to 2012.
- Records of patients above the age of 18 at the time of diagnosis and with a confirmed diagnosis either by histology, radiology or haematology.

Exclusion criteria

- Hospital records with incomplete data.

4.4. Sample size determination

The sample size was estimated according to Fisher's formula (Fisher 1991).

$$n = \frac{z^2 \hat{p}(1-\hat{p})}{m^2}$$

$$n = \frac{1.96^2 * 0.5(1-0.5)}{0.05^2}$$

n= 384

Where:

p = expected prevalence or proportion or estimated proportion of cancer in Kenya. This was the prevalence that was to be estimated by the study.

m= degree of precision or a tolerance error margin or width of the confidence interval (a measure precision of the estimate).

z= Z statistic for a level of confidence or is the normal distribution critical value for

a probability of $\alpha/2$ in each tail. For a 95% CI, z=1.96

For this study, a specified the level of confidence of 95%, an error margin of ±5% was considered acceptable, based on similar studies elsewhere.

The prevalence of cancer in Kenya is unknown therefore a prevalence of 50% was assumed in calculating the sample size.

Using this information in the sample size formula above a sample of **384** was estimated as the minimal necessary to achieve the required sufficient precision for the estimated prevalence.

4.5. Sampling technique

The sampling frame included records of patients diagnosed with cancer in the two referral hospitals who met the inclusion criteria. The sample size was distributed proportionately among the five year period. A systematic random sampling method was used to select patient's files. The first record was selected at random in every year. This first file was within the value of k. Subsequently, every k^{th} file was selected in an orderly manner to reach the required number.

Kenyatta National Hospital (KNH)

Year	Estimated number of files	Percentage of the total number of files	Files collected per year (n=500)
2008	3168	18%	90
2009	2834	16%	80
2010	3048	17%	85
2011	4161	24%	120
2012	4373	25%	125
TOTAL	**17,584**	**100%**	**500**

Moi Teaching and Referral Hospital (MTRH)

Year	Estimated number of files	Percentage of the total number of files	Files collected per year (n=500)
2008	947	22%	110
2009	1325	31%	154
2010	489	11%	57
2011	732	17%	85
2012	811	19%	94
TOTAL	**4304**	**100%**	**500**

The files available at KNH were for both the inpatients and outpatients and were all available at the Health Information Department. In MTRH the files available were for the inpatients and only 2012 files were available at the Health Information Department. Files for 2008 to 2011 were obtained at the oncology centre at AMPATH.

4.6. Data collection

After obtaining ethical approval and permission from the hospital directors, data was obtained from the patient's files from the medical records department of the above mentioned hospitals. A coded questionnaire was the study instrument used to abstract the information (Appendix 1). Patient's names were left out for the sake of confidentiality. Data was extracted from 2008 to 2012. Only the investigator and the research assistants had access to the files for the purposes of this study.

4.7. Data management and analysis

Data was abstracted from the patients file using a coded questionnaire (Appendix 1). All the questionnaires were reviewed by the principle investigator to ensure they were completed appropriately. Data collected was entered into an Excel spreadsheet in a password protected computer. Back-up copies were stored in an external hard drive and compact disc which were in sole custody of principal investigator.

The filled questionnaires were in the safe custody of the principal investigator who filed and stored them in a locked cabinet for verification during analysis.

Further cleaning was carried out after entry using frequency distributions and cross-tabulations until no more errors were detected.

The final step in the preparation for analysis was coding of the data and the creation of any composite variables from the cleaned data set.

In order to achieve the objectives of the study, data analysis which was done using Statistical Package for Social Sciences Programme (SPSS) version 17.0, was carried out using the following steps:

The Univariate analysis involved frequency distributions for categorical variables and descriptive statistics (means, medians, standard deviations) for continuous variables. Gender and referrals were presented in pie charts. Methods of cancer diagnosis, cancer types and residence were presented using bar charts and frequency distribution tables. Univariate analysis was used to give an understanding of the characteristics of the findings.

Bivariate analysis was used to investigate whether there was an association between gender and age and type of cancer. The χ^2 test was used to test association between 2 variables if they were categorical and satisfied all the conditions. If some χ^2 conditions were not met, Fisher's exact test was used instead.

4.8. Ethical considerations

Permission to carry out the research was obtained from the KNH/U.o.N. Ethics and Research Committee (Appendix 3). Permission to conduct the research at the hospitals was also obtained from the Director of Medical Services. Permission to extract data from the hospital registers and records was obtained from the Hospital directors of the hospitals participating in the study. The study was a minimal risk study since there was no direct patient involvement but a retrospective review of patients file. For confidentiality, the patients' files were only used within the confines of the medical records department of the above mentioned hospitals and only the investigator with the assistance of the medical records department personnel had the access to the files for the purposes of this study. Patient identifying information such as the names was not included in the data collection forms. All the filled questionnaires were stored in lockable drawers. Raw data inform of filled questionnaires, data stored in password protected computer or even the back-up copies in hard drives and compact disc were to be destroyed at the end of the study.

4.9. Study limitations

Although this study aimed to establish the burden of cancer associated with infectious agents, it is difficult to ascertain that a given cancer is specifically caused by an infectious agent.

The ability of some agents to remain latent, as well as the existence of new and emerging infections, makes detection and proving causality challenging. An infectious agent may trigger the initial events of oncogenesis but be absent in the final tumor, which adds timing of detection to the problem.

Under-reporting of cancer cases was a problem, MTRH lacked databases and the only cancer data available on their databases was that of 2012 and for the inpatients only. This made estimation of the total files per year and their tracing difficult and thus their study.

Limited space in the Health Information department was also a problem in this hospital limiting their storage capacity of files. A number of files in both hospitals were incomplete and important variables were left out thus rendering the files invalid for the study.

The data obtained from this study may not be generalizable and conclusive since people who come to the hospitals do not form a random sample. It was difficult to draw trends from this study since studies on trends are designed somewhat differently.

A total of four referral hospitals had been selected for the purpose of this study namely: Kenyatta National Hospital, Moi Teaching and Referral Hospital, Coast Province General Hospital and Jaramogi Oginga Odinga Teaching and Referral Hospital. Of these only two gave permission for the research to be conducted.

CHAPTER 5: RESULTS

5.1. KNH

5.1.1. DEMOGRAPHICS

A total of 17,584 (inpatient and outpatient) cancer cases were on follow up in KNH from 2008 to 2012. 500 files were sampled randomly. Of these, 60% were females and 40% were males (Figure 2). The mean age was 51 years (18 years to 95 years). 76.4% of patients were between the ages of 35 years to 74 years with the highest age group (55-64 years) with 22.8% (Figure 1).

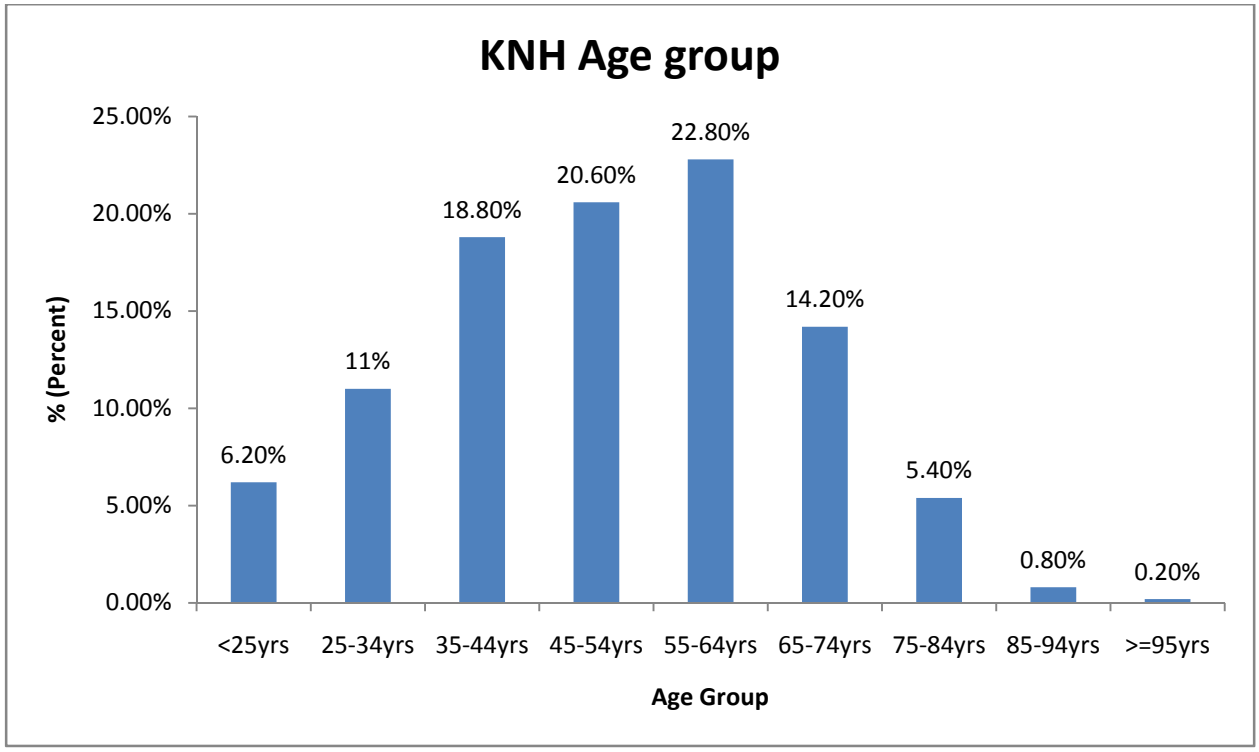

Figure 1: KNH Age distribution; x-axis represents the age group and y-axis represents the %. 76% of patients were between the ages of 35 years to 74 years with the highest age group (55-64 years) with 23%.

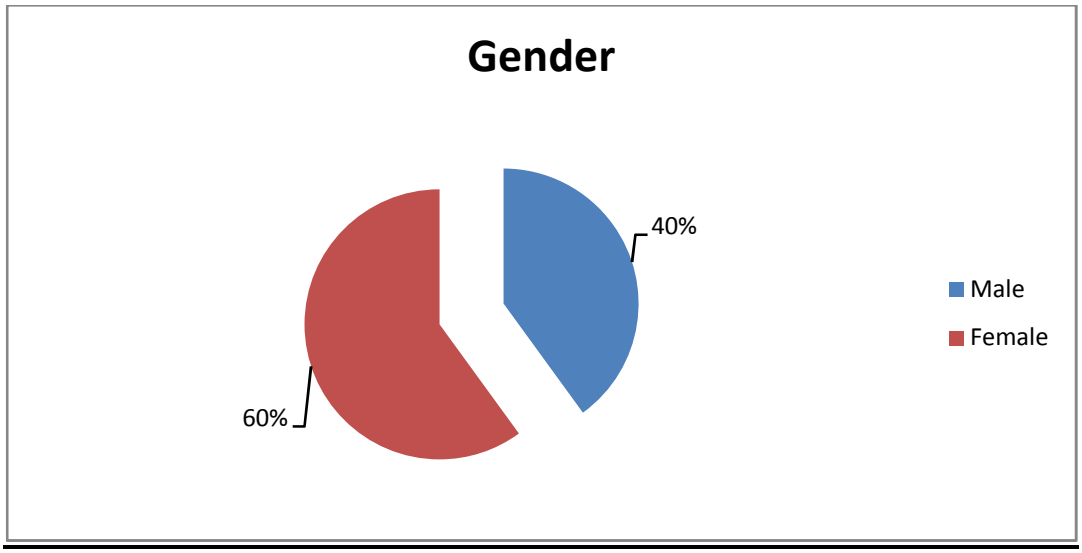

Figure 2: Gender of the study population at KNH; Females constituted 60% of the patients

Sixty six percent of these cancer cases were referrals from other hospitals of which 89% of these had histological confirmed diagnosis. Most cancer patients in KNH were by origin (place of birth) from Muranga, Kiambu, Machakos, Nyeri and Kisii (11%, 10%, 8%, 8% and 5.4% respectively) (Figure 3).

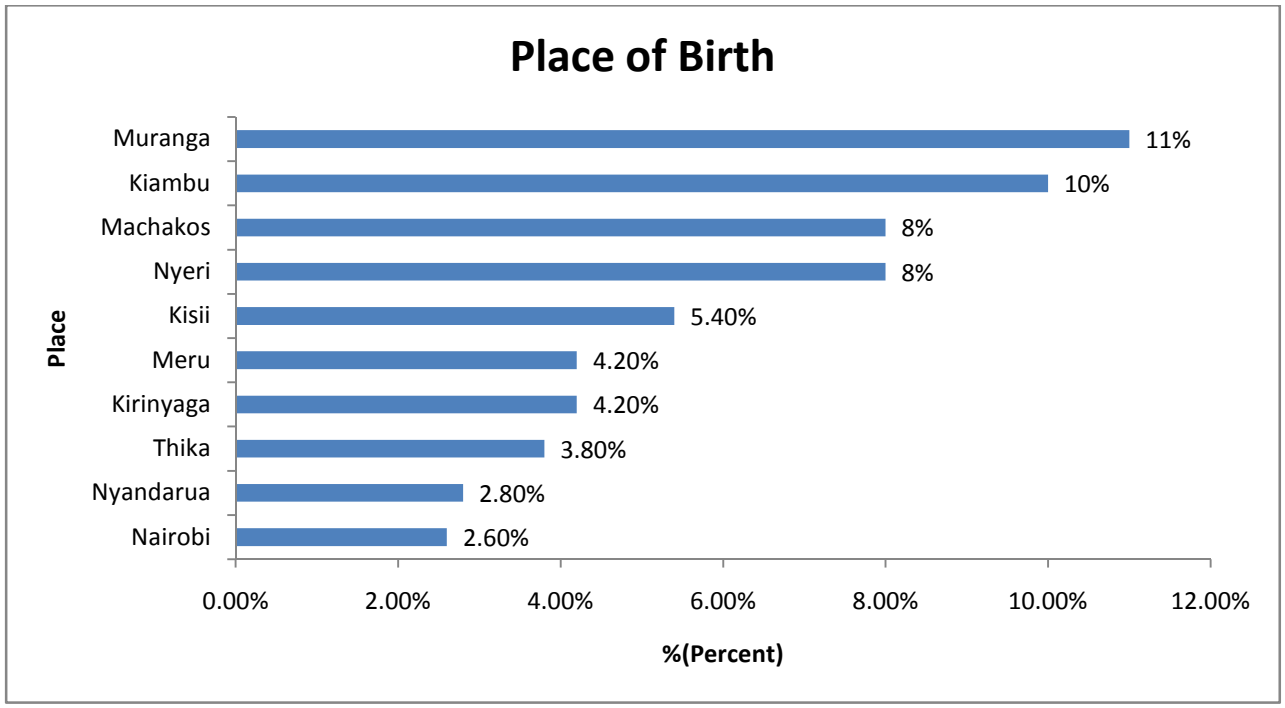

Figure 3: Place of birth of KNH study population; x-axis represents the % and y-axis represents the place of birth of the study population. Majority of the patients at KNH were from Muranga (11%), Kiambu (10%) and Machakos (8%).

5.1.2. TYPES OF CANCERS AT KNH

5.1.2.1. Common types of cancers at KNH

In both sexes (N=500), the five most common types of cancers were: cervical 62(12.4%), breast cancer 59(11.8%), leukemia 41(8.2%), colorectal 31(6.2%) then gastric 27(5.4%) (Figure 4, Table 1). In females (n=300) the five most common cancers were cervical 62(20.7%), breast 59(19.7%), leukemia 25(8.3%), ovary 22(7.3%) and gastric 15(5%). In males (n=200) the five most common types of cancers were prostate 23(11.5%), laryngeal 19(9.5%), colorectal 17(8.5%), leukemia 16(8.0%) and esophageal 14(7.0%) (Table 2).

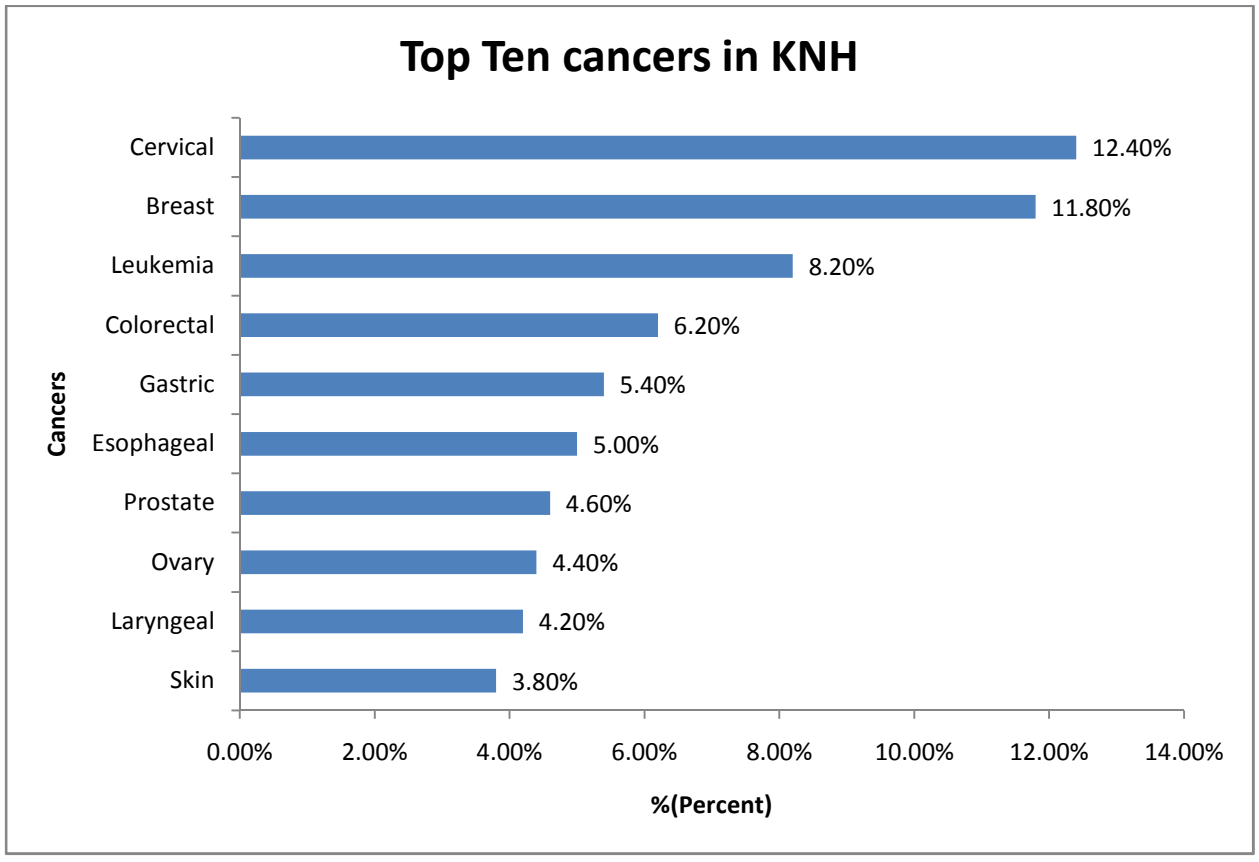

Figure 4: Top 10 cancers at KNH from 2008-2012 in both sexes; x-axis represents the % and y-axis represents the cancers. Cervical (12%) and breast cancers (11.8%) were the leading cancers at KNH

Table 1: All types of cancers at KNH from 2008-2012 in both sexes

Cancer prevalence in KNH (n=500)	N	%	95% CI
Cervical cancer	62	12.40%	(9.71,15.69)
Breast cancer	59	11.80%	(9.17,15.03)
Leukemia	41	8.20%	(6.02,11.05)
Colorectal cancer	31	6.20%	(4.32, 8.78)
Gastric cancer	27	5.40%	(3.66, 7.86)
Esophageal	25	5.00%	(3.33, 7.39)
Prostate cancer	23	4.60%	(3.00, 6.93)
Ovary	22	4.40%	(2.84, 6.69)
Laryngeal	21	4.20%	(2.68, 6.45)
Skin	19	3.80%	(2.37, 5.98)
Nasopharyngeal carcinoma	17	3.40%	(2.06, 5.50)
Endometrium	17	3.40%	(2.06, 5.50)
Others	17	3.40%	(2.06, 5.50)
Pancrease	14	2.80%	(1.60, 4.77)
Non Hodgkin's lymphoma	13	2.60%	(1.42, 4.56)
Lung and Bronchus cancer	11	2.20%	(1.16, 4.02)
Lip and Oral cavity	11	2.20%	(1.16, 4.02)
Hypopharyngeal	11	2.20%	(1.16, 4.02)
Liver cancer	10	2.00%	(1.13, 3.97)
Osteogenic	8	1.60%	(1.02, 3.77)
Bladder cancer	7	1.40%	(0.61, 2.99)
Thyroid	7	1.40%	(0.61, 2.99)
Genitalia	6	1.20%	(0.49, 2.73)
Eye	6	1.20%	(0.49, 2.73)
Multiple myeloma	6	1.20%	(0.49, 2.73)
Hodgkin's lymphoma	5	1.00%	(0.34, 2.43)
Parotid	4	0.80%	(0.26, 2.18)
Cholangiocarcinoma	4	0.80%	(0.26, 2.18)
Kaposi Sarcoma	2	0.40%	(0.07, 1.60)

Genitalia included penis, vagina, vulva and testis while others included renal, head, brain, anal, ear, rhabdomyosarcoma, meningioma, liposarcoma, nose, gluteal, choriosarcoma and pelvic cancers.

Table 2: Types of cancers at KNH by Gender from 2008-2012

Cancer Prevalence in KNH by Gender (n=500)	Sex	
	Male(200) n(%)	Female(300) n(%)
Gastric Cancer	12(6.0%)	15(5%)
Breast Cancer	0	59(19.7%)
Cervical Cancer	0	62(20.7%)
Colorectal cancer	17(8.5%)	14(4.7%)
Liver cancer	5(2.5%)	5(1.7%)
Lung and Bronchus cancer	8(4.0%)	3(1.0%)
Esophageal	14(7.0%)	11(3.7%)
Nasopharyngeal carcinoma	12(6.0%)	5(1.7%)
Lip and Oral cavity	6(3.0%)	5(1.7%)
Hodgkin lymphoma	2(1.0%)	3(1.0%)
Bladder cancer	5(2.5%)	2(0.7%)
Non Hodgkin's lymphoma	7(3.5%)	6(2.0%)
Prostate cancer	23(11.5%)	0
Kaposi Sarcoma	1(0.5%)	1(0.3%)
Leukemia	16(8.0%)	25(8.3%)
Skin	12(6.0%)	7(2.3%)
Osteogenic	6(3.0%)	2(0.7%)
Pancrease	7(3.5%)	7(2.3%)
Ovary	0	22(7.3%)
Endometrium	0	16(5.3%)
Genitalia	2(1.0%)	4(1.3%)
Eye	3(1.5%)	3(1.0%)
Hypo-pharyngeal	4(2.0%)	7(2.3%)
Laryngeal	19(9.5%)	2(0.7%)
Parotid	3(1.5%)	1(0.3%)
Thyroid	0	7(2.3%)
Cholangiocarcinoma	3(1.5%)	1(0.3%)
Multiple Myeloma	4(2.0%)	2(0.7%)
Other	10(5.0%)	7(2.3%)

Table 3: The most common malignancies diagnosed in different Age groups at KNH

Rank	Age	≤25	25-34	35-44	45-54	55-64	65-74	75-84	85-94	>=95
1		Osteogenic 12.9%	Leukemia 18.2%	Cervical Cancer 24.5%	Breast Cancer 17.5%	Breast Cancer 10.5%	Breast Cancer 8.5%	Prostate Cancer 22.2%	Gastric Cancer 25.0%	Gastric Cancer 100%
2		Leukemia 12.9%	Skin Cancer 9.1%	Breast Cancer 14.9%	Cervical Cancer 16.5%	Cervical Cancer 10.5%	Esophageal 8.5%	Gastric Cancer 18.5%	Prostate Cancer 25.0%	
3		Cervical Cancer 9.7%	Endometrium 7.3%	Leukemia 11.7%	Esophageal 7.8%	Colorectal 10.5%	Prostate 6.8%	Colorectal 14.8%	Laryngeal 25.0%	
4		Non Hodgkin's lymphoma 9.7%	Cervical Cancer 5.5%	Skin Cancer 4.3%	Colorectal 6.8%	Gastric Cancer 8.8%	Pancrease 8.5%	Esophageal 11.1%	Multiple Myeloma 25.0%	
5		Breast Cancer 6.5%	Non Hodgkin's lymphoma 5.5%	Ovary Cancer 4.3%	Ovary Cancer 5.8%	Laryngeal 8.8%	Endometrium 5.6%	Lip and Oral Cavity 11.1%		

5.1.3. PREVALENCE OF COMMON TYPES OF CANCERS AT KNH

Table 4: Prevalence of five common male cancers at KNH

Male Cancer Prevalence in KNH	2008	2009	2010	2011	2012
Leukemia	10.3%	18.9%	3%	5.9%	2.5%
Prostate Cancer	10.3%	8.1%	9.1%	17.6%	10%
Laryngeal	2.6%	8.1%	12.1%	13.7%	10%
Colorectal cancer	7.7%	10.8%	3%	11.8%	7.5%
Esophageal	10.3%	2.7%	9.1%	3.9%	10%

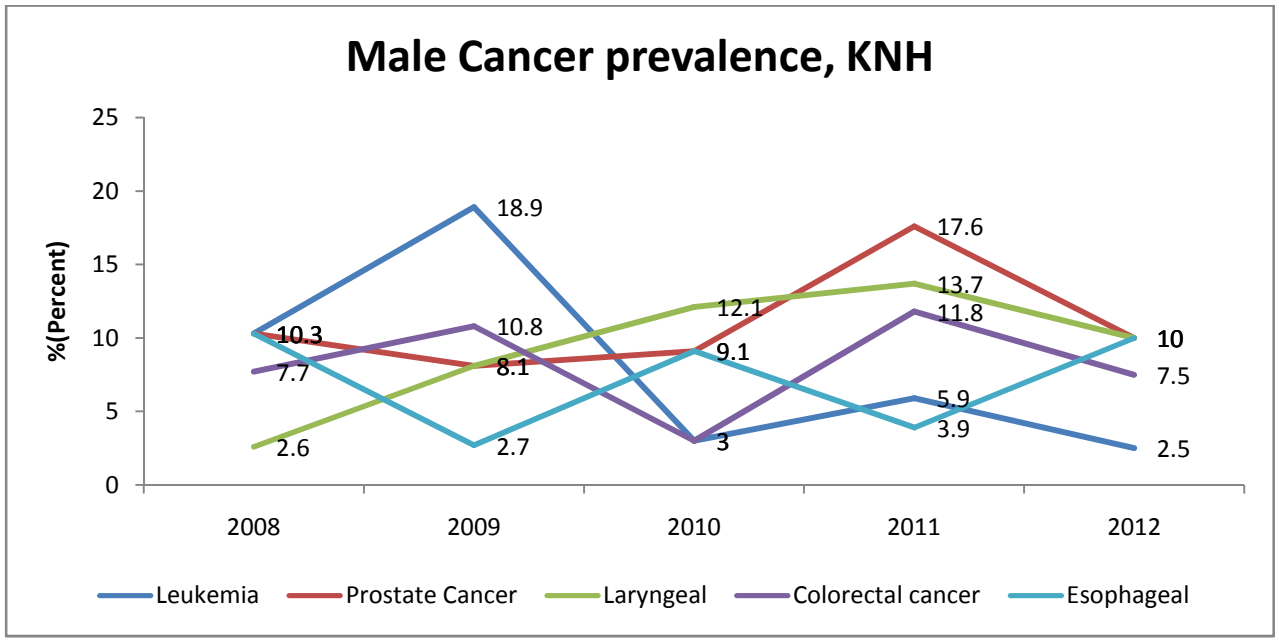

Figure 5: Prevalence of five common male cancers at KNH; x-axis represents the years and y-axis represents %.

Laryngeal and prostate cancer has been increasing from 2008 to 2011 with a slight decrease in 2012. There was a significant decrease in leukemia from (18.9%) in 2009 to (3%) in 2010 with a slight increase in 2011. Prostate was steady until 2011 where there was a significant increase (from 9.1% to 17.6%) with a decrease in 2012 (Figure 5).

Table 5: Prevalence of five common female cancers at KNH

Female Cancer Prevalence in KNH	2008	2009	2010	2011	2012
Gastric Cancer	3.9%	4.7%	3.8%	5.8%	5.9%
Cervical Cancer	19.6%	18.6%	21.2%	24.6%	18.8%
Breast Cancer	13.7%	14%	23.1%	20.3%	23.5%
Leukemia	15.7%	16.3%	3.8%	5.8%	4.7%
Ovary	5.9%	7%	5.8%	10.1%	7.1%

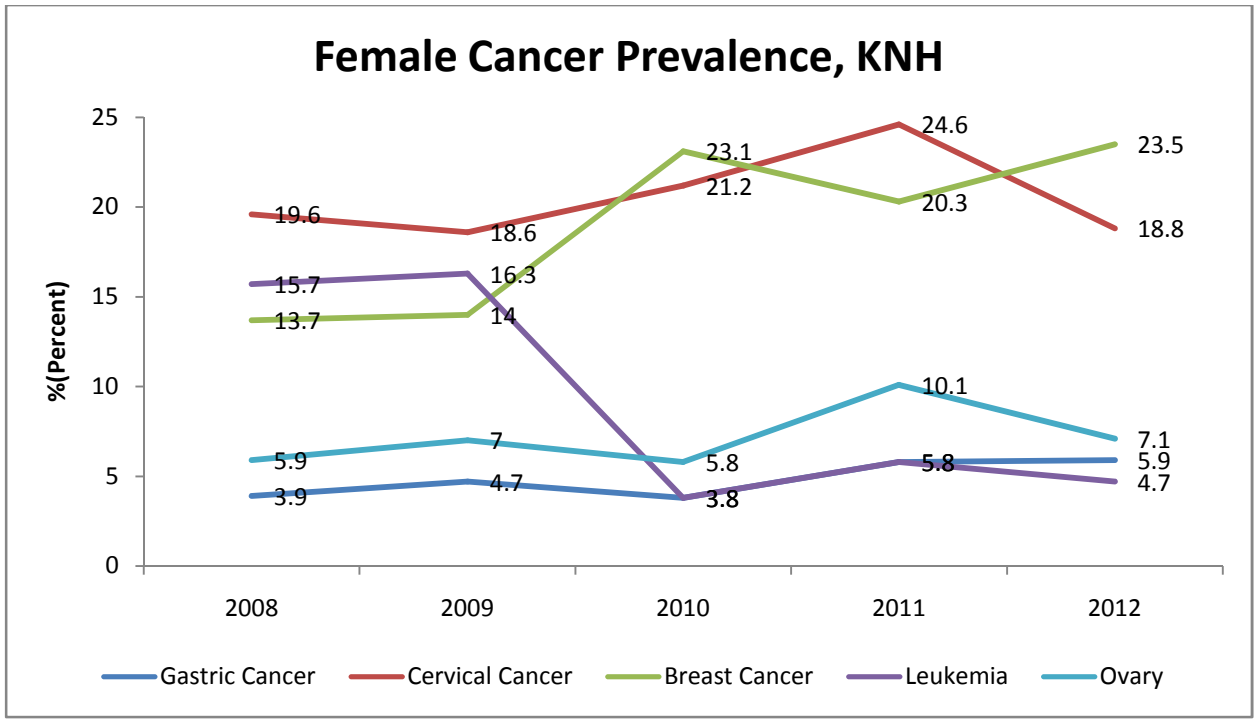

Figure 6: Prevalence of five common female cancers at KNH; x-axis represents the years and y-axis represents %

Breast and gastric cancers have been increasing over the years among the females. Cervical and ovarian cancers have been increasing with a slight decrease in 2012. There was an over ride between cervical and breast cancers along the years. Cervical cancer was leading in 2009, 2010 and 2011, whereas breast cancer took the lead in 2010 and 2011. There was a significant decrease in leukemia from (16.3%) in 2009 to (3.8%) in 2010 and a slight increase to 2012 (Figure 6).

5.1.4. CANCERS ASSOCIATED WITH INFECTIOUS AGENTS AT KNH

Among the cancers associated with infectious agents in both sexes from 2008 to 2012, the most prevalent cancers were cervical (12.4%), gastric (5.4%), Prostate (4.6%), nasopharyngeal carcinoma (3.4%), Non Hodgkin's Lymphoma (2.6%) and liver cancer (2.0%) (Figure 7).

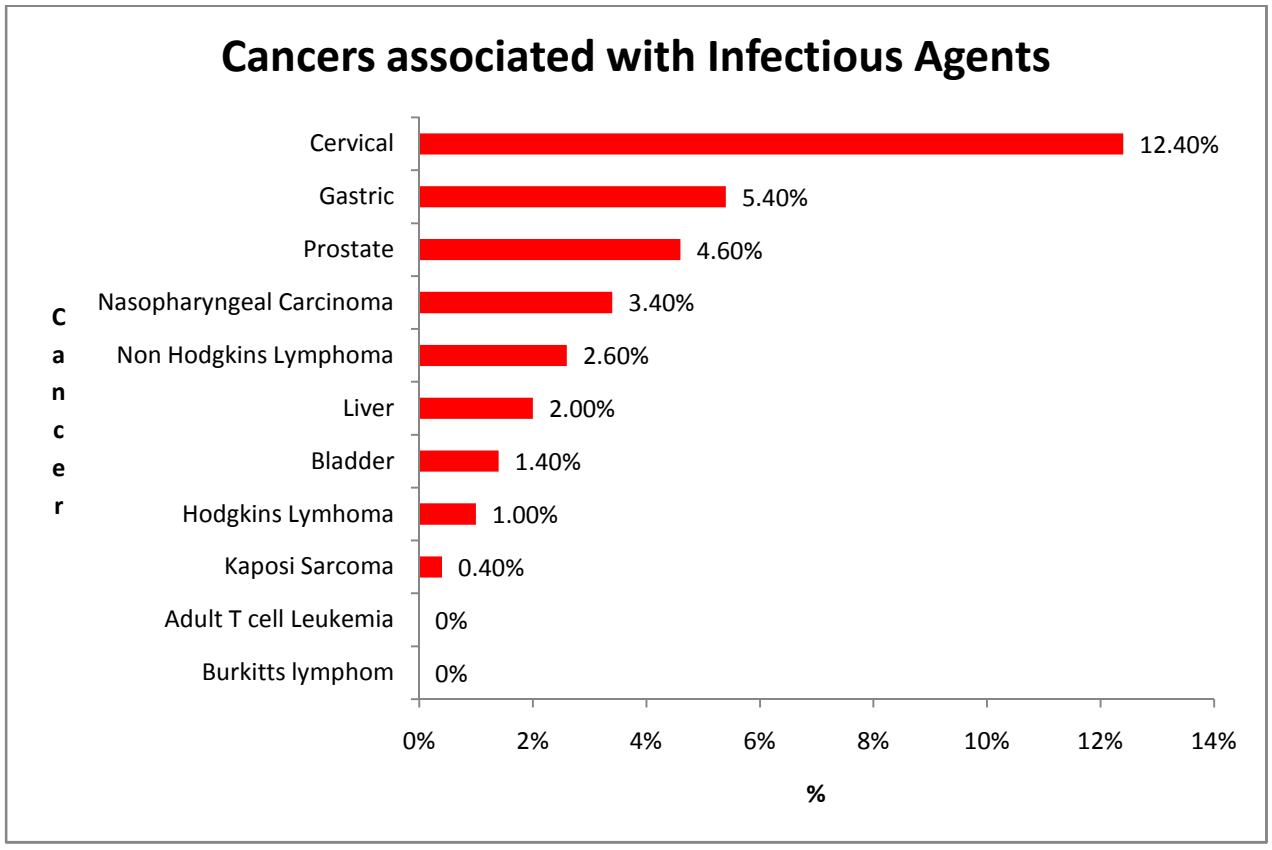

Figure 7: Top 10 cancers associated with infectious agents at KNH from 2008-2012 in both sexes; x-axis represents the % and y-axis represents the cancers. The most prevalent cancers were cervical (12%), gastric (5%), Prostate (4.6%), nasopharyngeal carcinoma (3%), Non Hodgkin's Lymphoma (2.6%) and liver cancer (2%)

5.1.5. PREVALENCE OF CANCERS ASSOCIATED WITH INFECTIOUS AGENTS

NHL among the males has shown an increased trend over the years. Gastric cancer has also been increasing over the years with a significant decrease in 2012 (Figure 8).

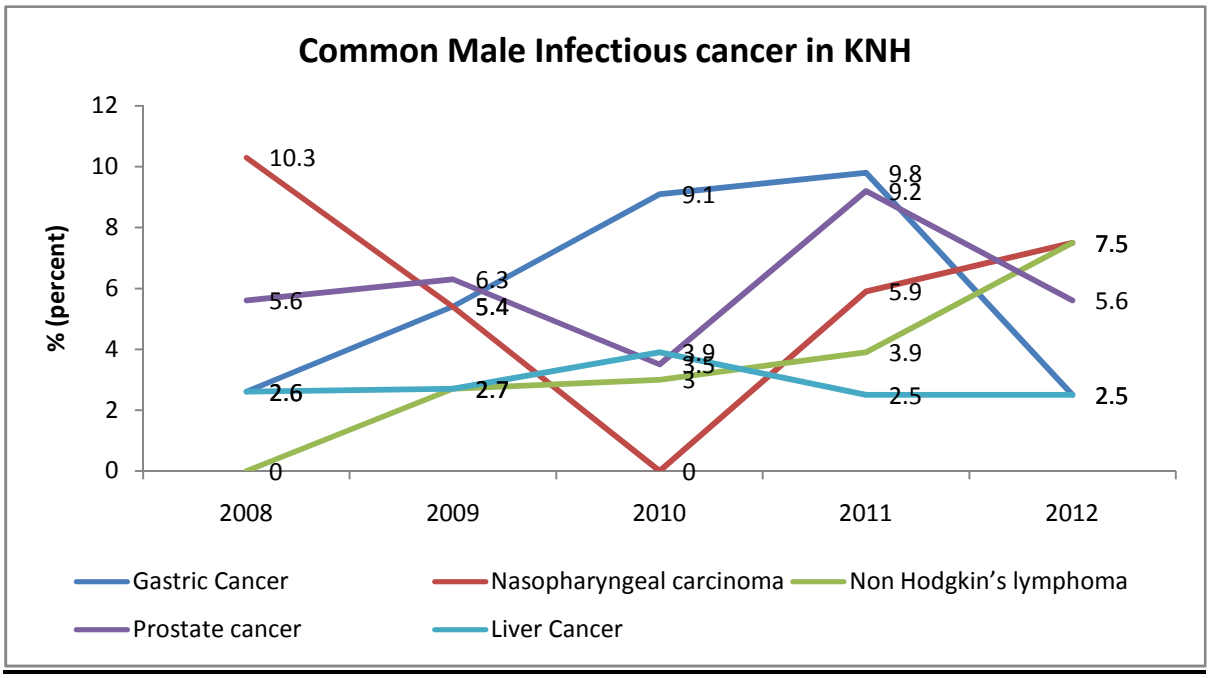

Figure 8: Prevalence's of the top 5 common male cancers associated with infectious agents; x-axis represents the years and y-axis represents %

Among the common cancers associated with infectious agents in females, there has been a steady trend with a slight decrease of cervical and nasopharyngeal carcinoma in 2012 (Figure 9).

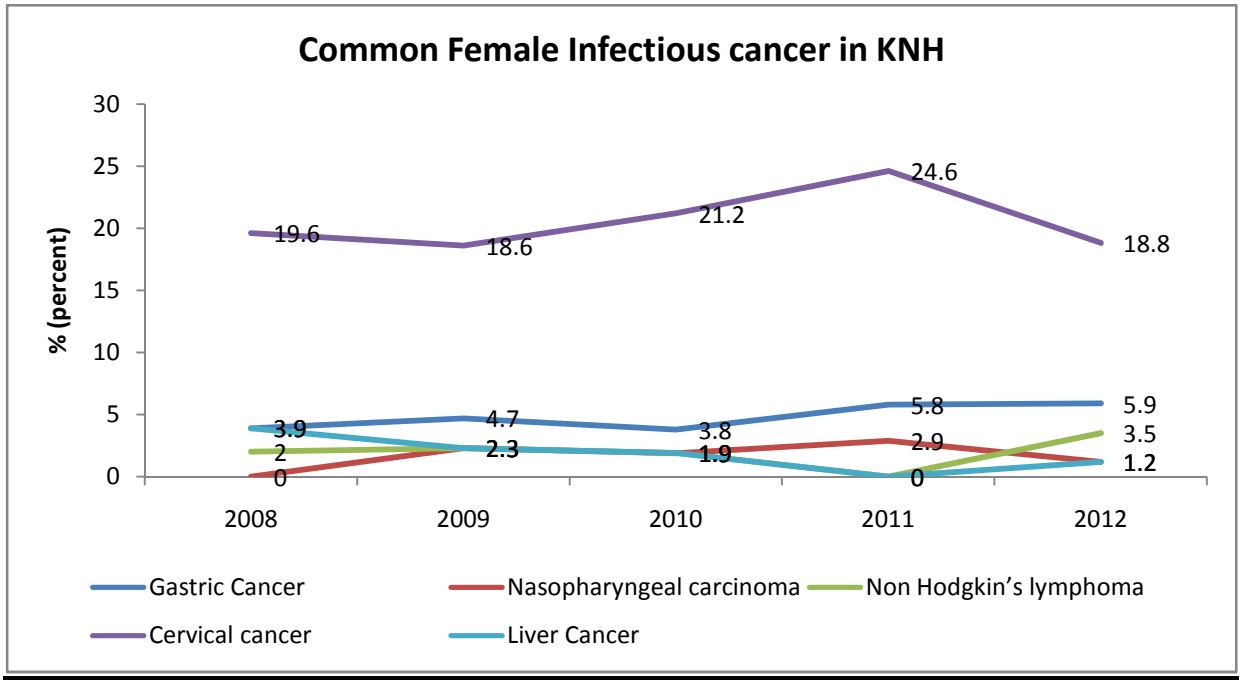

Figure 9: Prevalence's of the top 5 common female cancers associated with infectious agents. ; x- axis represents the years and y-axis represents %. Cervical cancer has been steadily increasing over the years

5.2. MTRH

5.2.1. DEMOGRAPHICS

A total of 4304 (inpatient only) cancer cases were on follow up in MTRH from 2008 to 2012. 500 files were sampled randomly. Of these 56% were females and 44% were males (Figure 2b). Mean age was 48 years (18years to 90 years). A majority of patients 76.6% were between 25 to64 years. Those aged 35 to 44 years had the highest percentage (22.8%) (Figure 1b).

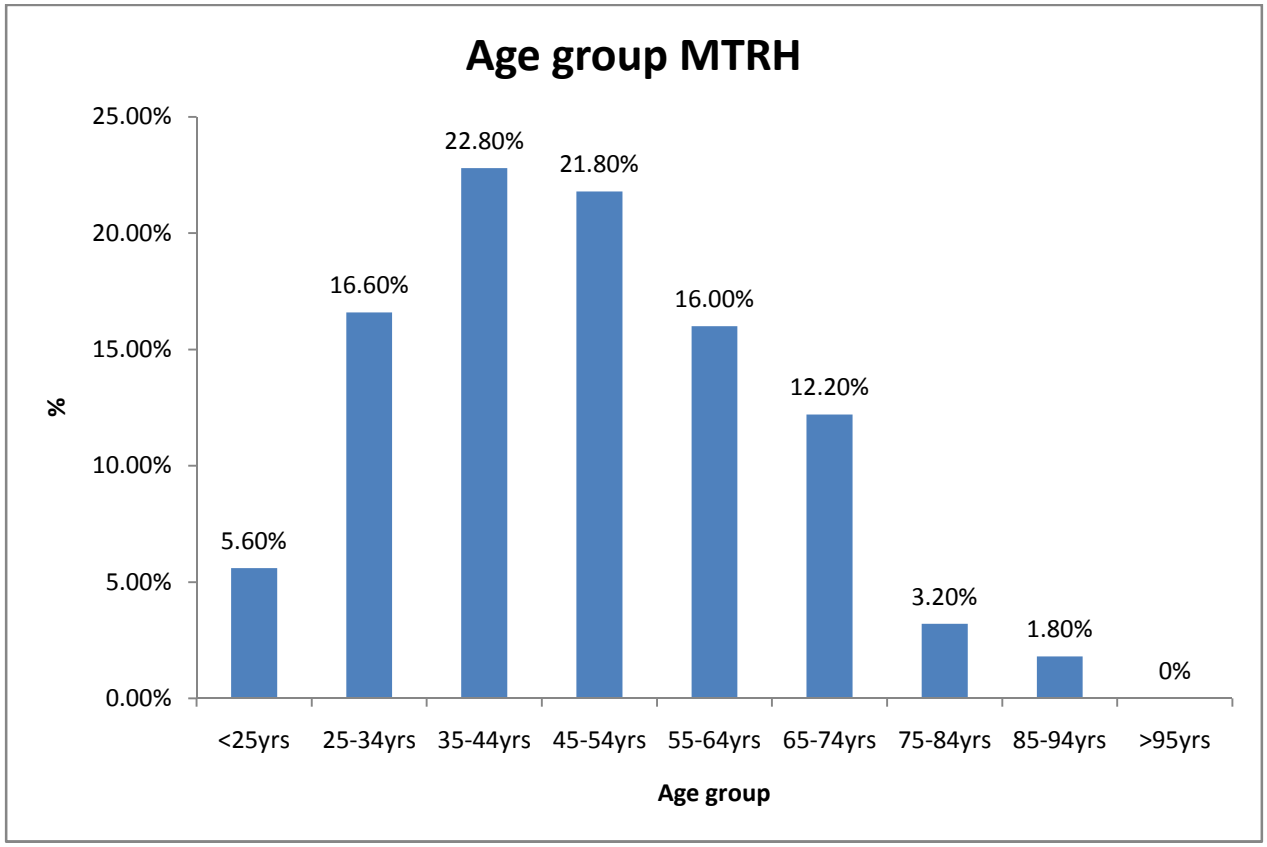

Figure 1b: Age distribution of MTRH study population; x-axis represents the age group and y-axis represents %. 77% of patients were between 25 to 64 years with the highest age group (35- 44 years) with (23%)

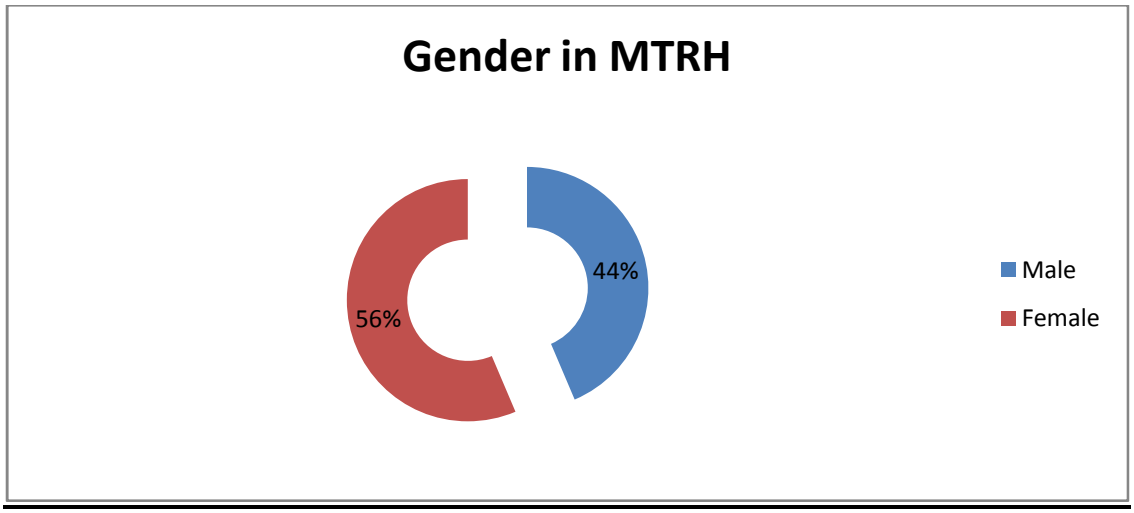

Figure 2b: Gender of study population at MTRH; Females constituted majority of the study population at 56%

Forty two percent of these cancer cases were referrals from other hospitals of which 91.2% of these had histological confirmed diagnosis. Most cancer patients in MTRH were by origin (place of birth) from Uasin Gishu, Nandi, Lugari, Trans Nzoia and Bungoma (22.8%, 8.4%, 8.4%, 7.4% and 6% respectively) (Figure 3b).

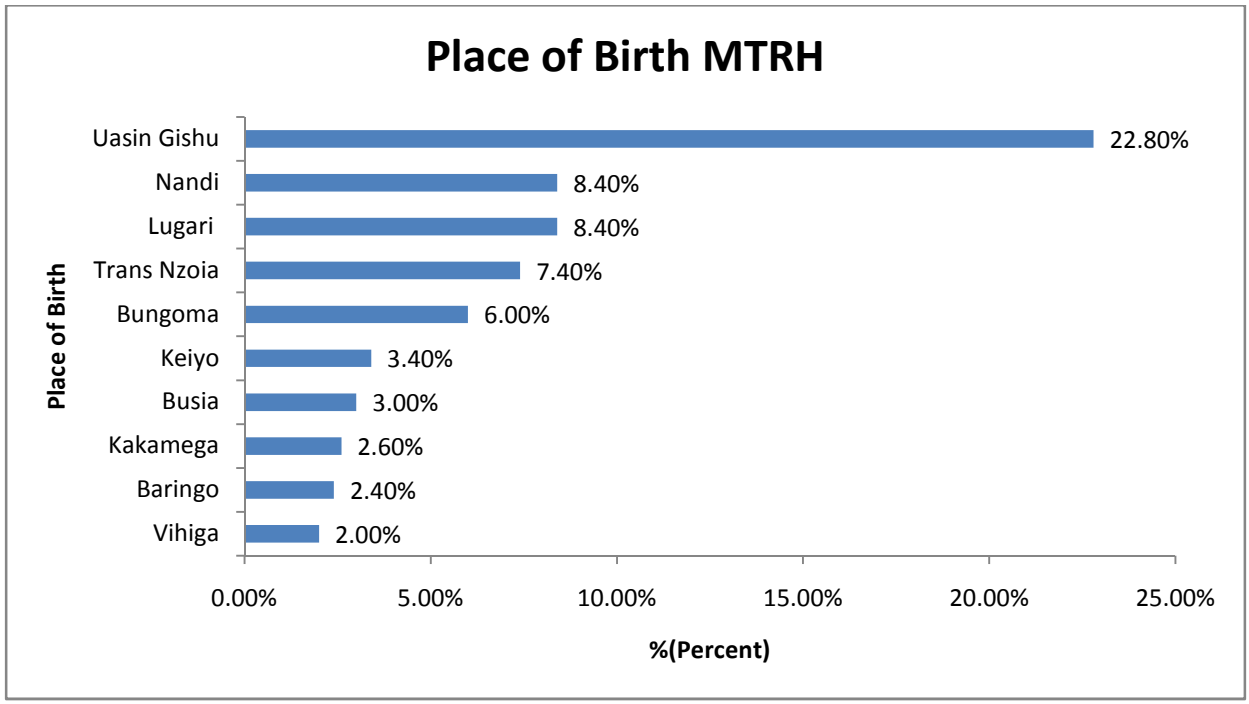

Figure 3b: Place of birth of MTRH study population; x-axis represents the % and y-axis represents the place of birth. Majority of the study population at MTRH were from Uasin Gishu (23%), Nandi (8%) and Lugari (8%)

5.2.2. TYPES OF CANCERS AT MTRH

5.2.2.1 Common types of cancers at MTRH

In both sexes (N=500) the five most common types of cancer were Kaposi sarcoma 93(18.6%), breast cancer 77(15.4%), cervical 43(8.6%), Non Hodgkin's Lymphoma 37(7.4%) and leukemia 36(7.2%) (Figure 4b). In females (n=282) the five most common types of cancers were breast cancer 74(26.2%), cervical 41(14.5%), Kaposi sarcoma 38 (13.5%), Non Hodgkin's Lymphoma 15(2.3%) and leukemia 15(5.3%). In males the five most common types of cancers were Kaposi sarcoma 55(25.2%), Non Hodgkin's Lymphoma 22(10.1%), leukemia 21(9.6%), colorectal cancer 16(7.3%) and esophageal cancer 16(17.3%) (Table 2b).

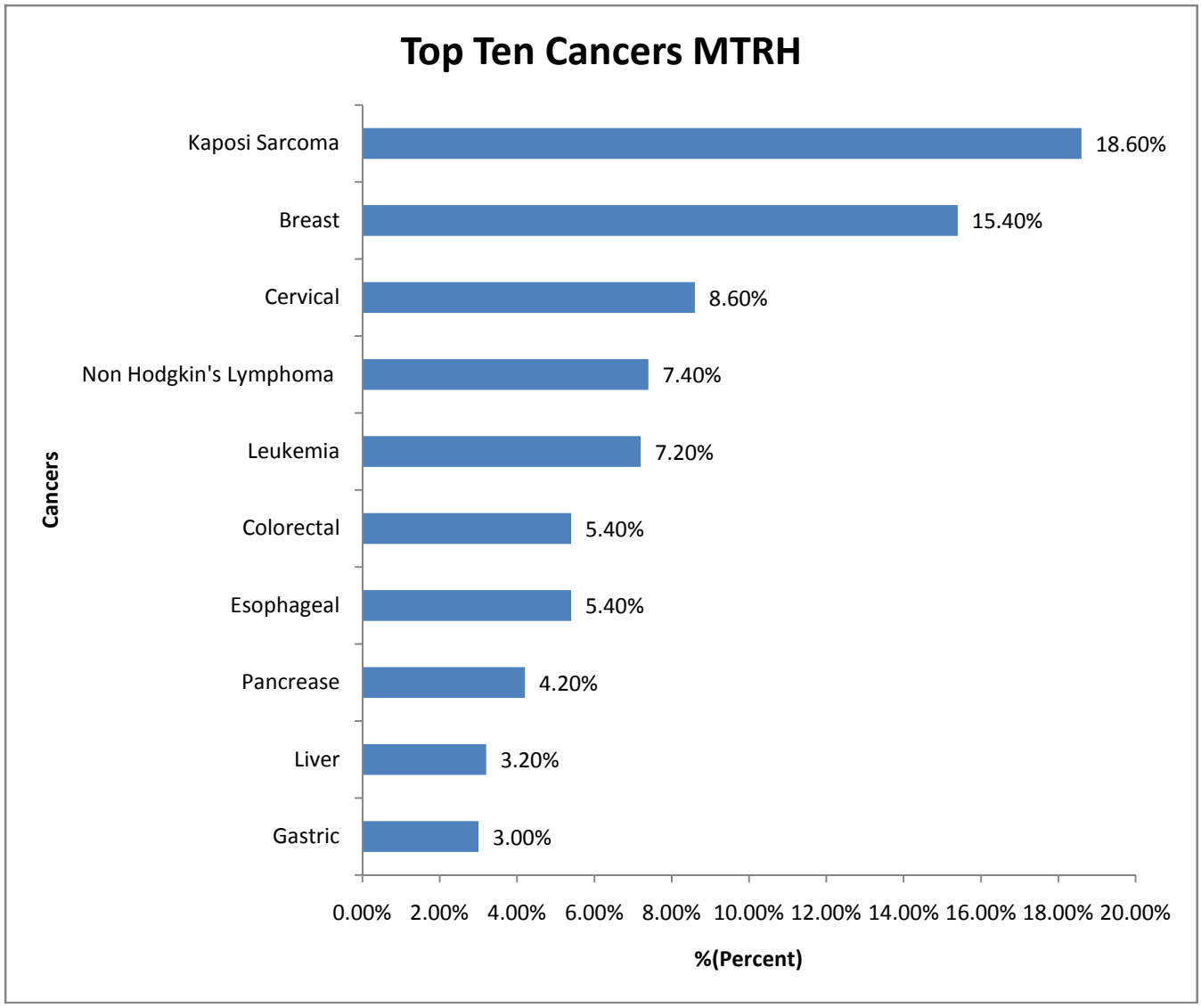

Figure 4b: Top ten cancers at MTRH in both sexes from 2008 to 2012; x-axis represents the % and y-axis represents cancers. Kaposi sarcoma (19%), Breast (15%) and Cervical cancer (9%) were the leading cancers at MTRH

Table 1b: All Types of cancer at MTRH in both sexes from 2008-2012

Cancer types in MTRH (n=500)	n	%	95% CI
Kaposi Sarcoma	93	18.60%	(15.34, 22.35)
Breast cancer	77	15.40%	(12.41, 19.93)
Cervical cancer	43	8.60%	(6.36, 11.50)
Non Hodgkin's lymphoma	37	7.40%	(5.57, 8.89)
Leukemia	36	7.20%	(5.16, 9.92)
Colorectal cancer	27	5.40%	(3.66, 7.86)
Esophageal	27	5.40%	(3.66, 7.86)
Pancrease	21	4.20%	(2.68, 6.45)
OTHERS	18	3.60%	(2.21, 5.74)
Liver cancer	16	3.20%	(1.90, 5.26)
Gastric cancer	15	3.00%	(1.75, 5.01)
Hodgkin's lymphoma	14	2.80%	(1.60, 4.77)
Ovary	14	2.80%	(1.60, 4.77)
Nasopharyngeal carcinoma	11	2.20%	(1.16, 4.02)
Skin	11	2.20%	(1.16, 4.02)
Multiple Myeloma	10	2.00%	(1.13, 3.97)
Lip and Oral cavity	9	1.80%	(0.88, 3.51)
Prostate cancer	7	1.40%	(0.61, 2.99)
Endometrium	5	1.00%	(0.34, 2.43)
Genitalia	4	0.80%	(0.26, 2.18)
Lung and Bronchus cancer	3	0.60%	(0.16, 1.90)
Laryngeal	3	0.60%	(0.16, 1.90)
Bladder cancer	2	0.40%	(0.07, 1.60)
Eye	2	0.40%	(0.07, 1.60)

Genitalia included penis, vagina, vulva and testis while others included renal, head, brain, anal, ear, rhabdomyosarcoma, meningioma, liposarcoma, nose, gluteal, choriosarcoma and pelvic

Table 2b: Types of cancers by Gender at MTRH from 2008-2012

Cancer Prevalence in MTRH by Gender (n=500)	Sex	
	Male	Female
	n=218	n=282
Gastric Cancer	5(1.4%)	10(3.5%)
Breast Cancer	3(1.4%)	74(26.2%)
Cervical Cancer	0	43(15.1%)
Colorectal cancer	16(7.3%)	11(3.9%)
Liver cancer	13(6.0%)	3(1.1%)
Lung and Bronchus cancer	1(0.5%)	2(0.7%)
Esophageal	16(7.3%)	11(3.9%)
Nasopharyngeal carcinoma	8(3.7%)	3(1.1%)
Lip and Oral cavity	4(1.8%)	5(1.8%)
Hodgkin lymphoma	7(3.2%)	7(2.5%)
Bladder cancer	1(0.5%)	1(0.4%)
Non Hodgkin's lymphoma	22(10.1%)	15(2.3%)
Prostate cancer	7(3.2%)	0
Kaposi Sarcoma	55(25.2%)	38(13.5%)
Leukemia	21(9.6%)	15(5.3%)
Skin	7(3.2%)	4(1.4%)
Pancrease	10(4.6%)	11(3.9%)
Ovary	0	14(5.0%)
Endometrium	0	5(1.8%)
Genitalia	1(0.5%)	3(1.1%)
Eye	1(0.5%)	1(0.4%)
Laryngeal	3(1.4%)	0
Multiple Myeloma	6(2.8%)	4(1.4%)
Other	9(1.4%)	9(3.2%)

Table 3b: The most common malignancies diagnosed in different Age groups at MTRH

Rank	Age	≤25	25-34	35-44	45-54	55-64	65-74	75-84	85-94	≥=95
1		Non Hodgkin's lymphoma 21.4%	Kaposi sarcoma 25.3%	Kaposi sarcoma 35.1%	Breast Cancer 20.2%	Breast Cancer18.8%	Breast Cancer 11.5%	Esophageal 18.8%	Pancrease 22.2%	
2		Kaposi's sarcoma 14.3%	Breast Cancer 12.0%	Breast Cancer 15.8%	Kaposi sarcoma 12.8%	Kaposi sarcoma 16.3%	Leukemia 11.5%	Lip and Oral Cavity 18.8%	Breast Cancer 11.1%	
3		Leukemia 10.7%	Leukemia 12.0%	Cervical Cancer 12.3%	Cervical Cancer 10.1%	Non Hodgkin's lymphoma 11.3%	Colorectal 9.8%	Prostate Cancer 12.5%	Cervical Cancer 11.1%	
4		Pancrease 10.7%	Cervical Cancer 8.4%	Leukemia 12.0%	Leukemia 8.3%	Esophageal 8.2%	Esophageal 8.8%	Breast Cancer 6.3%	Colorectal 11.1%	
5		Hodgkin's lymphoma 10.7%	Colorectal 8.4%	Colorectal 8.4%	Non Hodgkin's lymphoma 7.3%	Cervical Cancer 7.5%	Non Hodgkin's lymphoma 8.2%	Cervical Cancer 6.3%	Esophageal 11.1%	

5.2.3. PREVALENCE OF COMMON TYPES OF CANCERS AT MTRH

Table 4b: Prevalence of five common male cancers at MTRH

Male Cancer Prevalence's in MTRH	2008	2009	2010	2011	2012
Leukemia	10%	14.9%	5.9%	8%	3.8%
Kaposi Sarcoma	34%	31.1%	5.9%	28%	13.5%
Non Hodgkin's lymphoma	10%	10.8%	17.9%	12%	5.8%
Colorectal cancer	2%	10.8%	5.9%	4%	9.6%
Esophageal	6%	1.4%	0%	8%	19.2%

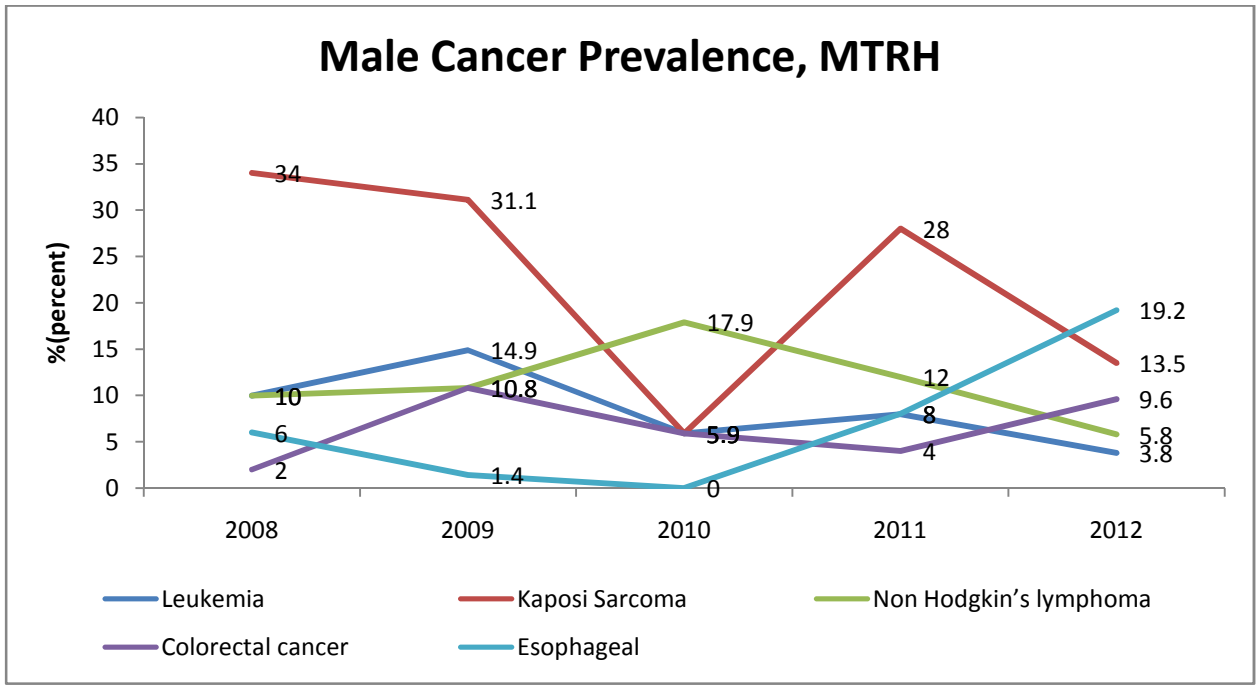

Figure 5b: Prevalence's of five common male cancers at MTRH; x-axis represents the years and y-axis represents the cancers.

In males Esophageal increased significantly from (0%) in 2010 to (19.2%) in 2012. NHL significantly decreased from 17.9% in 2010 to 5.8% in 2012. There was also a significant decrease in Kaposi's sarcoma from 31.1% in 2009 to 5.9% in 2010 for it to increase in 2011 (Figure 5b).

Table 5b: Prevalence of five common female cancers at MTRH

Female Cancer prevalence in MTRH	2008	2009	2010	2011	2012
Leukemia	8.3%	7.5%	0%	3.3%	4.8%
Cervical Cancer	5%	12.5%	20%	21.7%	16.7%
Breast Cancer	25%	23.8%	35%	33.3%	14.3%
Ovary	3.3%	1.3%	7.5%	11.7%	2.4%
Kaposi Sarcoma	26.7%	20%	7.5%	5%	0%

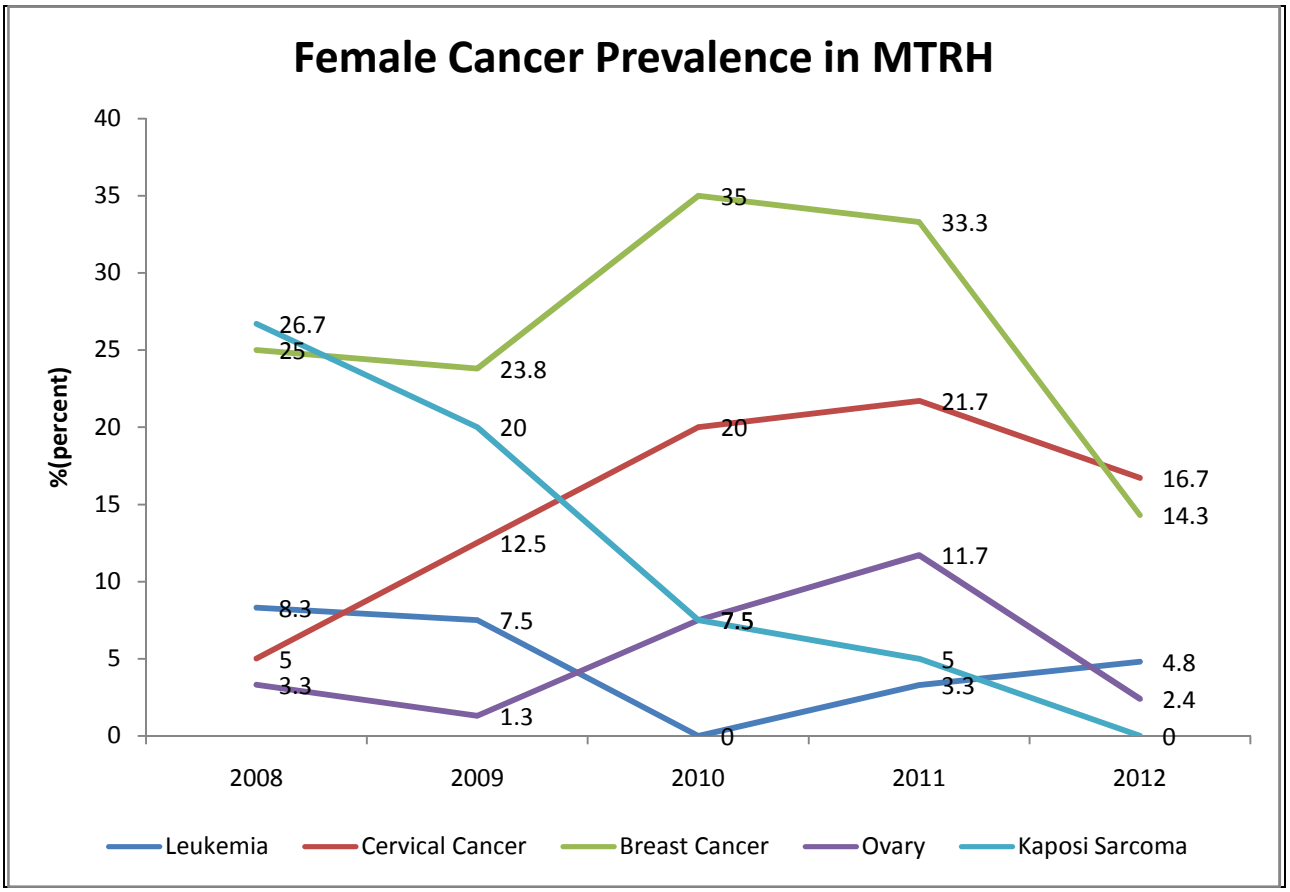

Figure 6b: Prevalence's of five common female cancers at MTRH; x-axis represents the years and y-axis represents the percentage

In females breast cancer was leading all through from 2008 to 2011 but was over ridden by cervical cancer in 2012. Ovarian cancer increased from 1.3% in 2009 to 11.7% in 2011 with a slight decrease in 2012. Kaposi sarcoma decreased significantly along the years (Figure 6b).

5.2.4. CANCERS ASSOCIATED WITH INFECTIOUS AGENTS AT MTRH

Among the cancers associated with infectious agents at MTRH, the five most common cancers were Kaposi's sarcoma (18.6%), Cervical (8.6%), Non Hodgkin's Lymphoma (7.4%), Liver (3.2%) and Gastric (3.0%) (Figure 7b)

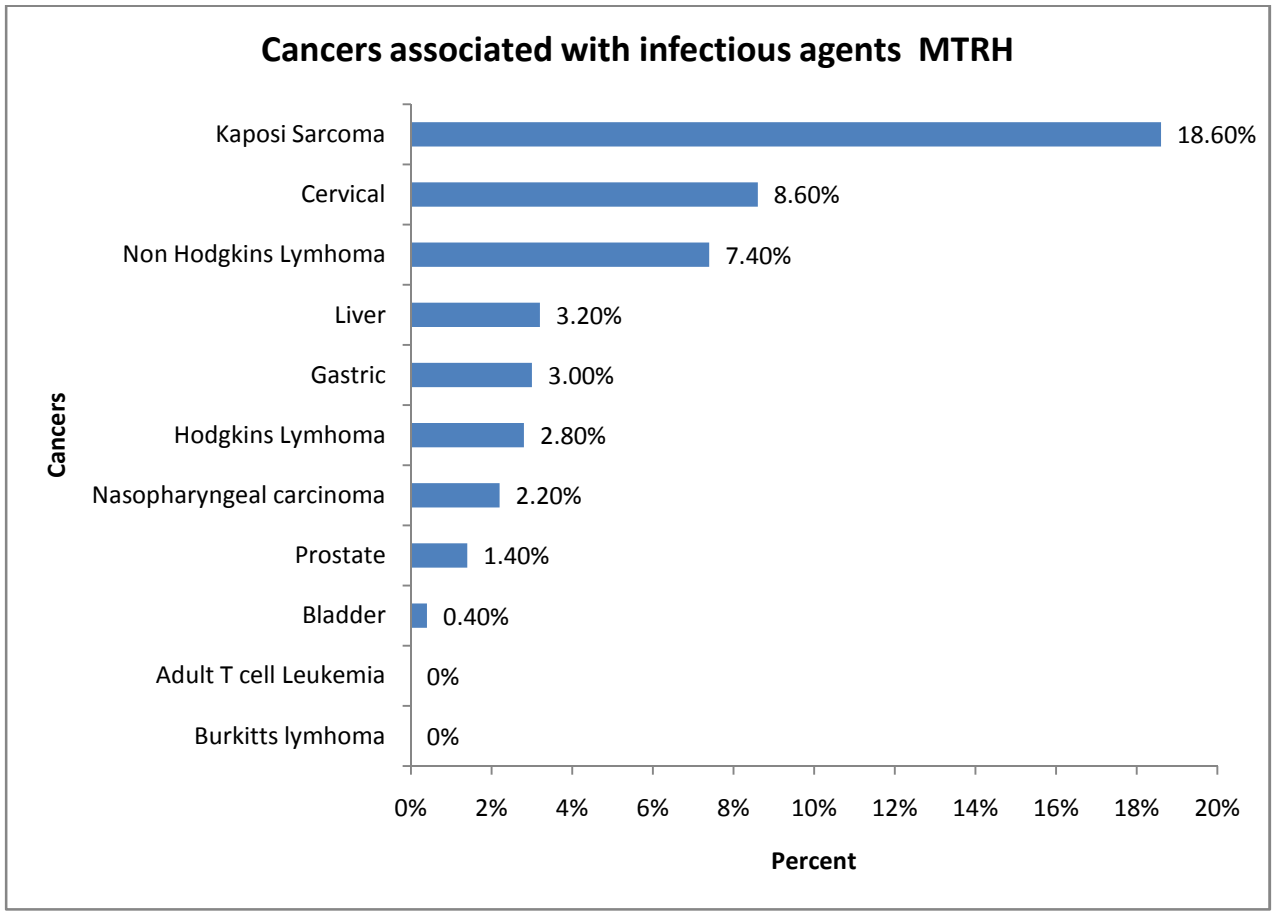

Figure 7b: Top ten cancers associated with infectious agents at MTRH in both sexes from 2008-2012; x-axis represents the % and y-axis represents cancers. Kaposi sarcoma, cervical cancer and Non-Hogkins lymphoma were the highest cancers associated with infectious agents

5.2.5. PREVALENCE OF CANCERS ASSOCIATED WITH INFECTIOUS AGENTS AT MTRH

In males, there was a significant decrease of Kaposi's sarcoma from 31.1% in 2009 to 5.9% in 2010 and a significant increase in 2011. Nasopharyngeal carcinoma remained steady but there was a significant decrease of HL from 11.8% in 2010 to 0% in 2011 and 2012.There was an increase in liver cancer from 2009 (Figure 8b)

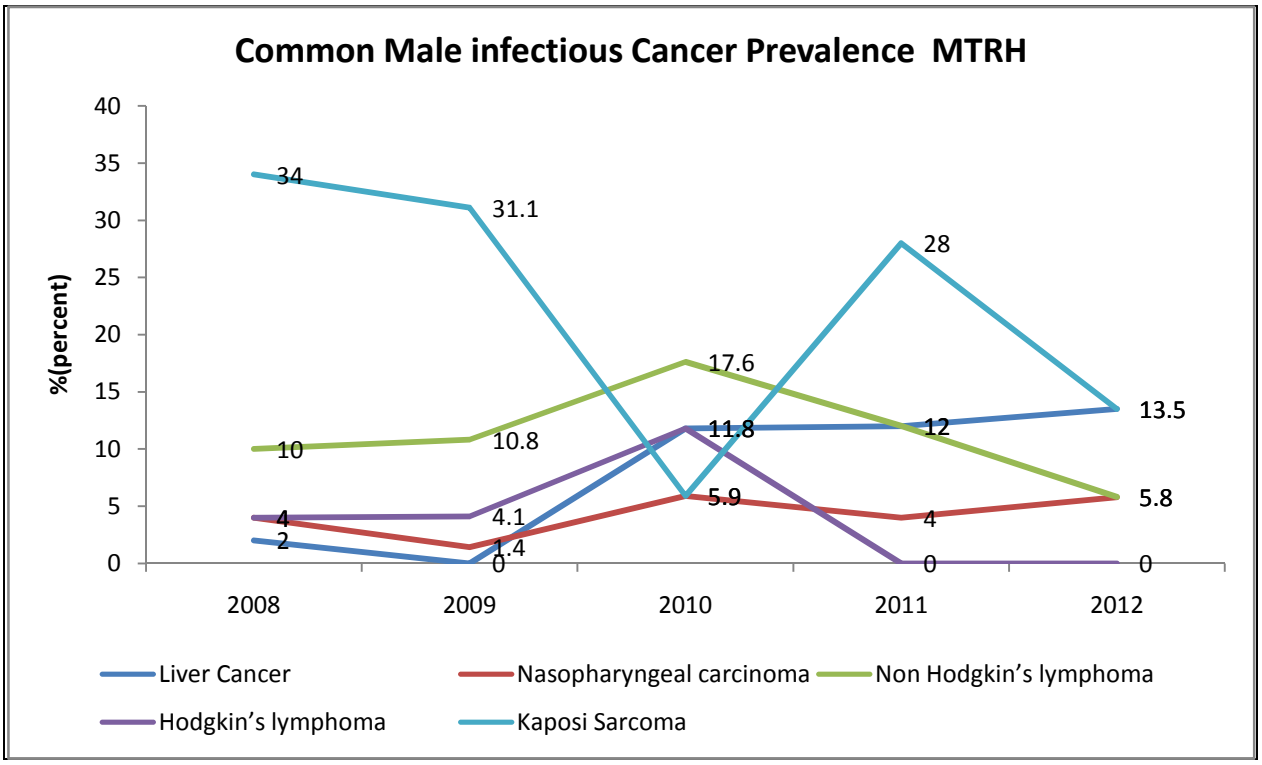

Figure 8b: Prevalence's of the top five male cancers associated with infectious agents; x-axis represents the years and y-axis represents the percentage

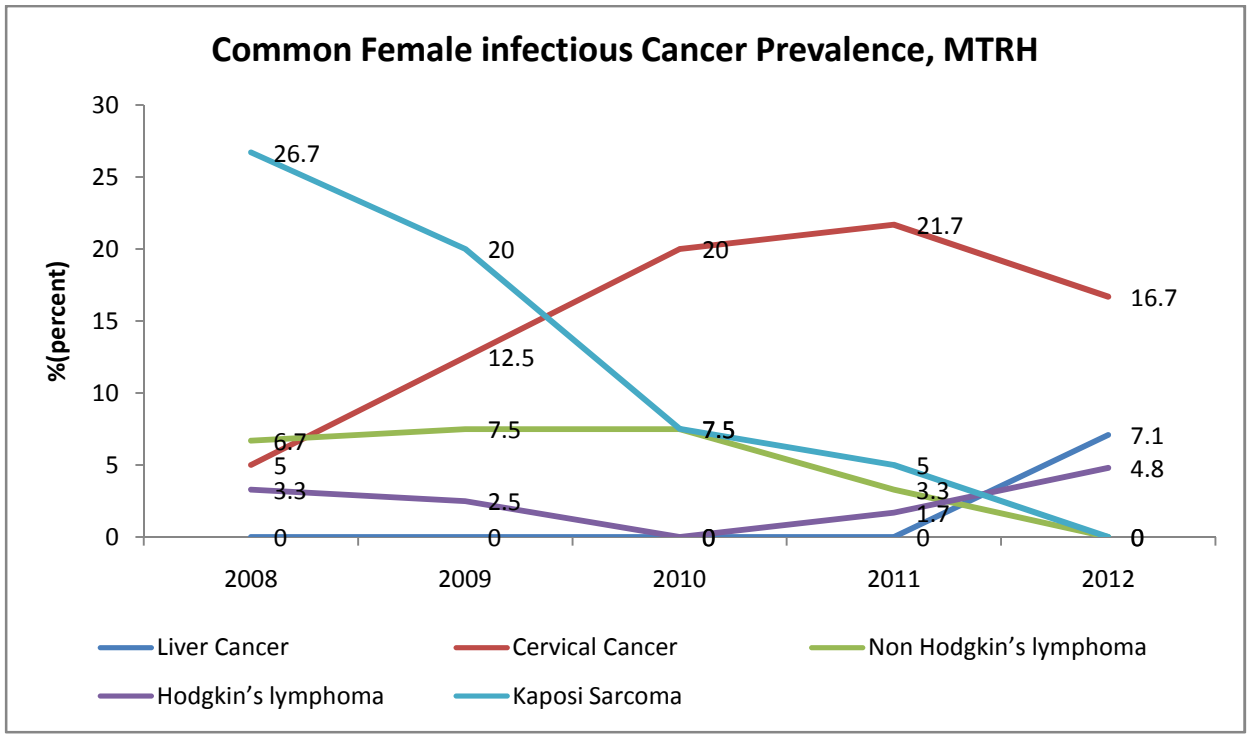

Figure 9b: Prevalence's of the top five female cancers associated with infectious agents; x-axis represents the years and y-axis represents the percentage

In females, Kaposi's sarcoma was decreasing along the years. Cervical cancer increased along the years with a slight decrease in 2012. Non Hodgkin's Lymphoma remained steady with a decrease from 2010. Liver cancer showed an increase in 2012 (Figure 9b).

CHAPTER 6: DISCUSSION, RECOMMENDATION AND CONCLUSION

6.1. DISCUSSION

This study conducted at two National referral hospitals in Kenya demonstrated that cancer is an important health problem in that KNH had 17,584 estimated number of patients (inpatient and outpatient) and 4304 in MTRH (inpatient). In KNH the top most cancers were cervical, breast cancer, leukemia, colorectal and gastric. In MTRH the top most cancers were Kaposi's sarcoma, breast cancer, cervical, Non-Hodgkin's Lymphoma (NHL) and leukemia.

In males the common cancers in both hospitals were colorectal, esophageal and leukemia. Kaposi's sarcoma and NHL were significantly high in males in MTRH while prostate cancer among the males in KNH. The high prevalence of KS, prostate and esophageal cancer is in line with the data from the Kenya National Cancer Control Strategy that showed that KS, prostate and esophageal cancer are the most common cancers in men (MOPHS & MOMS 2012). Similarly a retrospective study done in Tenwek Hospital in Western Kenya showed that the most common sites of cancer in men were esophagus, stomach, prostate and colorectal and NHL cancers (Parker et al., 2010). The low number of prostate cases in MTRH is particularly alarming especially with the free checkups available at this hospital. This would suggest that the reported number of prostate cases was likely under-reported because of the space issue at the records department to handle all the patients' files.

In females the common cancers in both hospitals were cervical, breast, ovary and leukemia. However gastric cancer was predominant in females in KNH while Kaposi's sarcoma was significantly high in females in MTRH. The high prevalence of breast, cervical and gastric cancer is in line with the data from the Western Kenya study that showed that the common sites of cancer in women were cervical, breast, stomach, uterus and esophagus (Parker et al.,

2010).This is also in line with a study done in sub-Saharan Africa that showed that some countries in East Africa have among the highest cervical cancer rates (50 cases per 100,000) worldwide (Ferlay et al., 2010). Breast cancer has become the most commonly diagnosed cancer in women in a study done sub-Saharan African countries, which also observed a shift between breast and cervical cancer rates though cervical cancer was the most commonly prevalent cancer in many of these countries (Mackay et al., 2006). This is also evident from what was observed from the trend curves. There was an override between cervical and breast cancer, with cervical cancer leading in 2008, 2009 and 2012 in KNH. Breast cancer was leading in MTRH but cervical cancer took the lead in 2012.The reasons for this shift may include increases in the prevalence of risk factors for breast cancer such as early menarche, late childbearing, having fewer children, obesity, awareness and detection (Jemal et al., 2011) .

Esophageal cancer was more prevalent in males than women in both KNH and MTRH. The reasons for the high prevalence among the males could be attributed to alcohol intake. Although studies show that esophageal is the leading cause of death among both men and women in East Africa (Jemal et al., 2011, Parker et al., 2010) this did not reflect in our study. However, the relative proportion of esophageal cases in comparison to other cases of cancer is higher at a study done in Tenwek Hospital. This may be due to increased patients' referrals and increased public awareness of esophageal care and palliation possibilities at Tenwek (Parker et al., 2010).

A study done in sub-Saharan Africa (Sasco et al., 2010) showed that infection with the Human Immunodeficiency Virus (HIV) entails an increased risk of developing AIDS defining diseases (KS,NHL, ICC) which were predominantly high in MTRH. Studies show that the incidence of KS has been steadily climbing in parallel with the AIDS epidemic in sub-Saharan Africa with a 20-fold increase in a study done in Uganda and Zimbabwe during the last 15 years making KS

the most common malignancy in men and the second most common in women following ICC in these regions (Bassett et al., 1995, Parkin et al., 1999). Other studies have shown cervical cancer to be highly prevalent in sub-Saharan Africa even before the HIV epidemic (Sasco et al., 2010). Another study conducted in Kenya among 3316 women diagnosed with ICC from 1989 to 1998 highlighted that the three-fold increase in HIV prevalence during this period was not followed by a similar trend concerning ICC (Gichangi et al., 2002).

This study revealed high cases of Leukemia in both hospitals. Although his high numbers would have been due to the fact that these cases were both for the acute and chronic types combined it was not clear why the numbers were high.

Among the cancer associated with the infectious agents, the most prevalent cancers in KNH were cervical, gastric, prostate, nasopharyngeal carcinoma, Non-Hodgkin's Lymphoma and liver cancer. The high burden of cervical, gastric and liver cancers are consistent with other studies that show that among infection-related cancers, stomach, liver and cervical cancer not only account for the vast majority of the total cancer burden associated with infections but they have the highest incidence(Parkin, 2006, Thun et al., 2010).

In MTRH the most prevalent cancers associated with infectious agents were Kaposi's sarcoma, Cervical, Non-Hodgkin's Lymphoma, Liver and Gastric. A study done by Msyamboza et al., 2012 also found out that KS was among the cancers causing the increased burden in Malawi (Msyamboza et al., 2012). Disparities in the prevalence rates of KS and NHL among the studied hospitals are likely the results of variations in the distribution of risk factors in these populations. Studies show that infection with HIV entails an increased risk of developing AIDS defining diseases (KS, NHL, CC) (Sasco et al., 2010). This could have been influenced by the fact that the oncology centre at MTRH is located at AMPATH (Academic model providing access to

healthcare) which offers treatment to HIV patients. KS and NHL have been decreasing steadily with a significant increase in KS among the males in MTRH in 2011. The reduction could have been influenced by HAART coverage that could have induced a significant difference. Studies show that, KS has been frequent in sub-Saharan Africa than in Western countries even before the HIV epidemic (Sasco et al., 2010).

The high numbers of cervical cancer observed in both populations is in line with the results obtained from Puerto Rico study (Ortiz et al., 2010): This could reflect a potential higher prevalence of HPV infection in these populations, low screening rates or late detection of the disease. This is particularly alarming especially with the free cervical checkups available at these hospitals. The mean age of patients with cervical cancer was 47 years and it could mean people go for these services when it's too late. The trends have been steadily increasing over the years with a slight decrease in 2012 for both populations. It could be that there was an increased use of cervical cancer screening from 2010 although they could also be influenced by decreasing patterns of HPV infections though the data on HPV is unavailable.

Differences in the prevalence rates of gastric cancer among the two populations were likely the results of variations in distribution of the risk factors in these populations. The higher prevalence of gastric cancer in KNH compared to MTRH suggests a higher prevalence of the risk factors in this population including infection with h. pylori (Plummer et al., 2004) increasing trend in males in KNH could be due to poor diet, *H.pylori*, poor hygiene, awareness or the stage of diagnosis. Although studies suggest that the age of at onset of infection is generally lower and peaks at 90% among young adults (Plummer et al., 2004), this is not the case at MTRH where the mean age was 57yers for males and 63 years for females). This could have translated to a late stage of diagnosis.

A higher number of liver cancer is observed among the males than females. This can be explained by higher prevalence of risk factors for liver cancer in men as compared to women such as higher alcohol consumption, HBV/HCV infections (Parkin, 2006). Although the data on HBV/HCV is scarce to accurately reflect the true proportion of people infected. Our study showed relatively consistent trends in the incidence of liver cancer in KNH and a slight increase among MTRH men and women. A possible explanation for the rising incidence could be due to an increase in the risk factors like alcohol.

Majority of patients were referrals from other places. This shows that majority of the patients have difficulty accessing cancer services resulting in long waiting times that could cause some previously curable tumors to progress to incurable stages. There was a common observation that female cases were more than males cases in both hospitals, this could be explained by the fact that probably males fear going to the hospitals or women tend to have frequent contact with the health professionals and show up in even greater numbers than men during health campaigns. The cancer types deferred between hospitals, this could have been explained by the files available at KNH were for both the inpatients and outpatients. In MTRH the files available were for the inpatients and only 2012 files were available at the Health Information Department. Files for 2008 to 2011 were obtained at the oncology centre at AMPATH which is an institution that deals with HIV/AIDS cases.

This study only collected and analyzed data that was already there. This provides local evidence that could be used to inform policies, strategies and interventions for prevention and control of cancer in Kenya.

6.2. RECOMMENDATION

- All files should be filled as required and all the information required captured making it easier to refer and study them.
- Digitize patients' files for easy access and safe keeping.
- All files should be stored safely and the information captured in databases in order to prevent under-reporting problems.
- Awareness should be increased by starting cancer education program in primary and secondary schools to create awareness at the grassroots to help reduce cancer cases.
- Health facilities should be welcoming to researchers by allowing research to be conducted so as to improve on policies.

6.3. CONCLUSION

This study demonstrated that the burden of cancer in Kenya is high and especially that associated with infectious agents that contribute to the overall burden. This could be explained by the low level of awareness, distant referrals, late detection of the cancers, expensive treatment options. Cancers especially those associated with infectious agents can be prevented or treated if identified early and reduction of these forms of cancers could translate to a significant reduction of the overall cancer burden in Kenya. Policies should be implemented and strategies enforced to increase the use of preventive measures such as increased awareness, vaccination, early and regular screening and treatment. Further research is warranted to establish the association of these cancers with the infectious agents as this may provide new avenues for effective cancer prevention.

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APPENDICES

APPENDIX 1: DATA COLLECTION FORM

TOPIC: **BURDEN OF CANCER ASSSOCIATED WITH INFECTIOUS AGENTS AT FOUR REFERRAL HOSPITALS, KENYA**

QUESTIONNAIRE NUMBER: …….

SITE

1. Kenyatta National hospital (KNH) ☐
2. Moi Teaching and Referral Hospital (MTRH) ☐
3. Coast Province General Hospital ☐
4. Jaramogi Oginga Odinga Teaching and Referral Hospital ☐

PATIENT GENERAL INFORMATION

Age of patient…….

Sex Male ☐

Female ☐

Patient's origin (place of birth)……

Was the patient a referral?

Yes ☐ No ☐

If so specify……..

PATIENT MEDICAL HISTORY

1. **Type of cancer**

List of common types of cancers

Gastric cancer	☐	Breast cancer	☐
Cervical cancer	☐	colorectal cancer	☐
Liver cancer	☐	Lung and Bronchus cancer	☐
Esophageal	☐	Nasopharyngeal carcinoma	☐
Burkitt's lymphoma	☐	Lip and Oral cavity	☐
Hodgkin's lymphoma	☐	Bladder cancer	☐
Non Hodgkin's lymphoma	☐	Prostate cancer	☐
Adult T cell leukemia	☐	Kaposi Sarcoma	☐
Leukemia	☐	Skin cancer	☐
Osteogenic	☐	Pancrease	☐
Ovary	☐	Endometrium	☐
Eye	☐	Hypopharyngeal	☐
Laryngeal	☐	Parotid	☐
Thyroid	☐	Cholangiocarcinoma	☐
Genitalia (Penis, Vaginal, Vulva, Testis)			☐
Multiple myeloma	☐		

OTHERS ☐ Specify……

2. **Method of cancer diagnosis used**.

1. **Biopsy** ☐

2. **Aspiration** 2.1.Fine needle aspiration ☐

2.2. Bone marrow aspiration ☐

3. **Blood test** ☐

4. **Pap smear** ☐

5. **Radiological/Imaging**

5.1. X-ray ☐

5.2. Computed Tomography (CT) ☐

5.3. Magnetic Resonance Imaging (MRI) ☐

5.4. Ultrasound ☐

5.5. Mammogram ☐

OTHERS ☐ Specify……

3. Year of diagnosis

Year 2008 ☐

Year 2009 ☐

Year 2010 ☐

Year 2011 ☐

Year 2012 ☐

APPENDIX 2: TABLES

Table 6:Leading causes of death in developing and developed countries, in thousands: 2004

	Developing			Developed		
	Rank	**Deaths**	**%**	**Rank**	**Deaths**	**%**
Heart diseases	1	7342	14.5	2	1563	19.3
Malignant neoplasms	2	5255	10.4	1	2154	26.6
Cerebrovascular diseases	3	4949	9.8	3	757	9.4
Lower respiratory infections	4	3910	7.7	4	305	3.8
Perinatal conditions	5	3141	6.2		35	0.4
Chronic obstructive pulmonary disease	6	2737	5.4	5	285	3.5
Diarrhoel diseases	7	2148	4.2		14	0.2
HIV/AIDS	8	2018	4.0		20	0.2
Tuberculosis	9	1448	2.9		15	0.2
Road traffic accidents	10	1158	2.3		114	1.4
Diabetes mellitus		914	1.8	7	221	2.7
Malaria		888	1.8		0	0.0
Suicide		707	1.4	9	118	1.5
Liver cirrhosis		655	1.3	10	116	1.4
Nephritis and nephrosis		611	1.2	8	126	1.6

Source: World Health Organization, The global burden of disease: 2004 update

Table 7: Estimated New Cancer Cases & Deaths for leading cancer sites in Developing countries, 2008

Estimated new cases				**Estimated Deaths**			
Male		**Female**		**Male**		**Female**	
Lung & bronchus	612,500	Breast	691,300	Lung & Bronchus	539, 000	Breast	268,900
Stomach	466,900	Cervix uteri	453,300	Liver	402,900	Cervix uteri	242,000
Liver	440,700	Lung & Bronchus	272,000	Stomach	353,500	Lung & Bronchus	239,000
Colon & rectum	274,000	Stomach	247,000	Esophagus	223.000	Stomach	202,900
Esophagus	262,600	Colon & rectum	232,400	Colon & rectum	154,400	Liver	177,700
Prostrate	255,000	Liver	186,000	Prostate	121,900	Colon & rectum	134,100
Urinary bladder	119,500	corpus uteri	144,900	Leukemia	95,100	Esophagus	115,900
Leukemia	116,500	esophagus	137,900	Non-Hodgkin lymphoma	71,600	ovary	75,700
Oral cavity	107,700	ovary	125,200	Nervous system	63,700	leukemia	75,100
Non-Hodgkin lymphoma	103,800	leukemia	93,400	Oral cavity	61,200	Nervous system	50,300

Source: GLOBOCAN 2008

APPENDIX 3: APPROVAL

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

KNH/UON-ERC
Email: uonknh2erc@uonbi.ac.ke
Website: www.uonbi.ac.ke
Link:www.uonbi.ac.ke/activities/KNHUoN

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

KENYATTA NATIONAL HOSPITAL APPROVED 4 JUN 2013 ETHICS RESEARCH COMMITTEE

Ref: KNH-ERC/A/151

4th June 2013

Macharia Lucy Wanjiku
Dept. Medical Microbiology
School of Medicine
University of Nairobi

Dear Lucy

RESEARCH PROPOSAL: BURDEN OF CANCER ASSOCIATED WITH INFECTIONS AGENTS AT FOUR REFERRAL HOSPITALS, KENYA (P24/01/2013)

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 June 2013 to 3rd June 2014.

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.

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET
Tel: 33471/2/3

Reference: IREC/2013/134
Approval Number: 0001027

25th July, 2013

Ms. Lucy Wanjiku Macharia,
Nairobi University,
School of Medicine,
Department of Microbiology,
P.O. Box 30197- 00202,
NAIROBI-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
APPROVED
25 JUL 2013
P.O. Box 4606 ELDORET

Dear Ms. Macharia,

RE: FORMAL APPROVAL

The Institutional Research and Ethics Committee have reviewed your research proposal titled:-

"Burden of Cancer Associated with Infectious Agents at Four Referral Hospitals, in Kenya."

Your proposal has been granted a Formal Approval Number: ***FAN: IREC* 1027** on 25th July, 2013. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 24th July, 2014. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc:	Director	-	MTRH
	Principal	-	CHS
	Dean	-	SOM
	Dean	-	SPH
	Dean	-	SON
	Dean	-	SOD

INTERNAL MEMO
Kenyatta National Hospital

OFFICE OF THE ASSISTANT DIRECTOR – HEALTH INFORMATION

KNH/HI/23-ADM/VOL.2 **Date ; 14th June, 2013**

TO WHOM IT MAY CONCERN

Dear Sir/Madam

RE: LETTER OF SUPPORT FOR MACHARIA LUCY

The department of Health information has received the request by the Principal investigator (Macharia Lucy) and will allow her to conduct research on "the Burden of cancer associated with infectious agents" using the records in our department. The study has already been approved by KNH/ERC committee

Kindly assist where applicable.

Yours sincerely,

CHIEF MEDICAL RECORDS OFFICER
Kenyatta National Hospital

M.O MUDENYO
AD-HEALTH INFORMATION SERVICES

MOI TEACHING AND REFERRAL HOSPITAL

Telephone: 2033471/2/3/4
Fax: 61749
Email: director@mtrh.or.ke
P. O. Box 3
ELDORET

Ref: ELD/MTRH/R.6/VOL.II/2008

23rd August, 2013

Ms. Lucy Wanjiku Macharia,
Nairobi University,
School of Medicine,
Department of Microbiology,
P.O Box 30197-00202,
NAIROBI-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
APPROVED
23 AUG 2013
P.O. Box 4606 ELDORET

RE: APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:-

"Burden of Cancer Associated with Infectious Agents at Four Referral Hospitals, in Kenya".

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

DR. J. KIBOSIA
DIRECTOR
MOI TEACHING AND REFERRAL HOSPITAL

CC - Deputy Director (CS)
- Chief Nurse
- HOD, HRISM