

Service-Learning Project/Directed Research:

The causes and clinical treatment for hepatocellular carcinoma in The Gambia: a study at the Royal Victoria Teaching Hospital

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Abstract

Hepatocellular carcinoma (HCC), also known as hepatoma, is a common cancer worldwide and a prevalent cause of death in Sub-Saharan Africa. The main causes for HCC in The Gambia are the hepatitis B virus and dietary aflatoxin consumption. Hepatitis B is endemic to The Gambia, and as a result horizontal transmission occurs during young childhood and through sexual transmission; approximately 15% of Gambians are hepatitis B carriers. Aflatoxins are toxic carcinogenic metabolites of mold found in groundnuts, maize and grains, which are causes of liver complications when consumed at moderate levels during a lifetime. In this study aside from the main causes of HCC, I explore the impact traditional medicine and the lack of health awareness has on the development of HCC. Generally, ailing individuals consult traditional healers before seeking clinical treatment and the added burden of not being aware of how to properly prevent and/or treat the illness decreases the likelihood of suffering individuals to consult a medical doctor. Finally, I highlight the clinical treatment for HCC patients involving the laboratory tests requested, characteristics that the patients exhibit and symptoms. I also emphasize the challenges and obstacles doctors at RVTH encountered while caring and treating for HCC patients.

Key words: Hepatocellular carcinoma, treatment, The Gambia, Royal Victoria Teaching Hospital

Introduction

Preliminary Introduction

Hepatocellular carcinoma (HCC), also known as hepatoma, is a common cancer worldwide and a prevalent cause of death in Sub-Saharan Africa (Bosch et al. 2005). In The Gambia, HCC has been defined as the most rampant form of cancer. The overall age standardized incidence rate (ASR) per 100,000 individuals for males and females within the Gambian population is 61.0 and 55.7, respectively, according to the data collected from the Gambian National Cancer Registry (Bah et al. 2001). Generally, individuals that subsequently develop HCC initially experience complications of liver cirrhosis which are caused by a number of viral, environmental and personal health factors. The incidence rate of HCC is alarmingly high in The Gambia and raises concern about the safety and well-being of men, women and young children. The Hepatitis B virus (HBV) is a predominant risk factor because it is endemic to The Gambia (Bah et al.2006). Approximately 15% of Gambian adults are chronic carriers of the virus (Kirk et al.2004). Aside from the influence of HBV, the Gambian population is faced with yet another influential cause of HCC. The exposure to aflatoxin, a toxin which is found in ground nuts (peanuts) and maize, increases the possibility for developing complications of the liver and ultimately may lead to HCC (Kuniholm et al.2008). Since ground nuts are a favorable ingredient used in local food dishes, this increased consumption makes individuals more susceptible to adverse complications.

Beyond the scope of causes, the current action for reducing the occurrence of HCC is essential – treatment. By creating the sufficient means for treating individuals with the disease, there should be a change in the number of fatalities. The level of causation, personal choice and treatment vary from individual to individual within the population, but the end result is the same – death. Why is this? The Gambia is the smallest and one of the most underdeveloped countries in

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Africa, so the influence of low socioeconomic status and underdeveloped infrastructure may present an issue in the progression of development. However, The Gambia is home to a number of developing medical and health facilities where skilled and trained professionals care for individuals with acute and chronic medical conditions. With the burden of HCC as a common cause of death, doctors must prevail in spite of the circumstance of limited supplies and equipment. Through research and personal curiosity, I was motivated to ascertain the effectiveness and quality of clinical treatment in The Gambia for individuals that are suffering from HCC.

In this paper, I will discuss my observations and findings for the causes and clinical treatment of HCC in The Gambia from the study I conducted at the Royal Victoria Teaching Hospital (RVTH). I found the hepatitis B virus as the foremost cause and aflatoxin as a secondary contender of HCC. I also highlighted the influence and contribution of non-pathogenic causes such as traditional medicine and lack of awareness regarding liver cancer health. Most importantly, this study was done to emphasize the challenges, yet perseverance shown by the doctors I encountered who were clinically treating HCC.

Service-Learning Site: Royal Victoria Teaching Hospital

The Royal Victoria Teaching Hospital (RVTH) in Banjul, The Gambia is a medical institution that strives to achieve an environment conducive for local and international research by various agencies. RVTH was once the Royal Victoria Hospital (RVH); it is the oldest and largest hospital in the country. In the late 1990's the University of The Gambia (UTG) was created, with the medical school as its first active educational faculty. The RVTH was slowly transformed from a basic hospital into a teaching hospital. The Gambian government has worked steadily to create an educational facility to train, teach and prepare Gambians to become experts in various medical fields rather than depending on foreign doctors (<http://www.rvth.org/main.htm>). Therefore RVH

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partnered with the University of The Gambia (UTG) to accommodate the School of Medicine and Allied Health Sciences. In the effort to improve healthcare in The Gambia, medical students are introduced to clinical experience and therefore obtain the expertise and communication skills to ultimately transform the quality of patient care provided (<http://www.rvth.org/main.htm>). The expansion of RVH to RVTH facilitated an increase in local medical research efforts.

More importantly, the clinical objective for RVTH is to supply and maintain sufficient health services to the public, perform accurate tests and investigations and strive to effectively implement treatment plans for patients. RVTH has 548 beds for patient care and attends to an average of 23,846 in-patients per year. The main departments that comprise the hospital are Pediatrics, Gynecology, Mental Health services, Infectious Diseases and a polyclinic that focuses on Primary healthcare. Within these wards, doctors, nurses and trainees - medical and nurse students, work diligently to attend to patients and provide the utmost care (<http://www.rvth.org/main.htm>).

Why RVTH?

RVTH has established a foundation that has continued to improve its clinical development over the past several decades. The hospital can treat the largest number of patients country wide and therefore treats a high number of individuals suffering from HCC or pre-related symptoms and/or conditions of HCC. In The Gambia, HCC age-adjusted rates are 34 and 11 per 100,000 individuals in males and females, respectively (Bah et al.2006).

Unfortunately, a number of patients admitted to RVTH have liver related issues, either caused by HBV, exposure to aflatoxins and/or overconsumption of iron and alcohol. The female and male internal medicine wards accommodate these patients, just as well as many other common ailments such as stroke, diabetic foot and tuberculosis (TB). The percentage of individuals admitted RVTH with HCC serves as an opportunity to learn about the disease first-hand, how it manifests

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and the complications that arise. It is an environment conducive for gathering raw information about the types of treatment for HCC, as well as its quality and effectiveness. The ease of accessibility in and out of the wards is very beneficial. Being able to witness examinations, observe one-on-one patient and doctor interactions and freely communicate with doctors among different departments presents the perfect opportunity to gather relevant data. I am also welcomed in the record-keeping department that specifically houses information on cancer - liver cancer. This is fundamental for evaluating treatment of HCC on an analytical and statistical level and will therefore further support my findings. There is little restriction and restraint on who I am able to speak with, where I am able to go and what I am able to do. Hence, a place that is welcoming to new research and assistance is an ideal environment to conduct my study. Shadowing a doctor who is managing HCC patients permits the opportunity to assess the efficiency of clinical treatment for HCC in The Gambia.

A personal insight of my choice

Whilst RVTH caters to its patients, the intent to educate prospective medical students, nurses and doctors is important as well. Doctors and medical staff are willing to establish a network of doctors in related fields and encourage care and handling of patients for students in training or conducting research. Since RVTH is the largest hospital in The Gambia, which is not too far from my living quarters in Kanifing, I wanted to seize the opportunity to fulfill my professional and personal objectives. Because RVTH is responsible for treating and caring for 648 patients daily, doctors encounter patients suffering from a range of minor illnesses to terminal diseases such as HIV/AIDS (<http://www.rvth.org/main.htm>). It is an ideal place that permits a novice medical researcher, like myself, the opportunity to learn and discover more about clinical medicine and the culture of Gambia within the walls of a medical institution and the system of clinical treatment. With regard to my research, I had access to first-hand resources – the doctors that treat the illness.

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Their guidance and direction would stimulate a different level of learning through research – application. Although inexperienced with no certified training, my thoughts and opinions of the patient diagnosis would be acknowledged and considered which is not only gratifying but instills a sense of togetherness. Aside from my research focus, I would be exposed to an immense spectrum of illness and disease which is an excellent opportunity to learn and discover across different medical disciplines. Furthermore, I would be exposed to the system of hospital operation and patient protocol, which is essential to know in any line of health or medical profession. I ultimately plan to become a medical researcher and earn a doctorate in public health, so the clinical experience is an exceptional way for establishing a foundation in medicine.

The Gambian culture is riveting, enriched with traditional values, morals and ethics; I wanted to experience the culture in a different environment – the hospital. Exploring how culture and conventional medicine merge in a society where traditional medicine and other forms of treatment are sought after as a therapeutic agent would stimulate my personal curiosity. This is a way to gauge my intellect and understand more about the human condition. Exposure at RVTH would teach medicine in ways no American medical institution would. Initially, I hoped to work closely with a doctor specializing in the hepatitis B virus and/or liver cancer in order to obtain sufficient information about the clinical treatment of HCC. By both reviewing daily records and documents of patients I would be able to explore exactly why, in most cases, patients with liver problems that are admitted to RVTH are in the final stages of the illness. I want assess the characteristics and compare the symptoms patients exhibit in order to ascertain a clearer understanding for the severe condition upon admission to the hospital. What are the obstacles and challenges doctors must overcome to prolong the life these patients? What are the initial measures taken to treat the patient? Depending on the stage of cancer, what is the clinical protocol for

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treating the patients after the initial diagnosis? In addition to viewing written sources, I hoped to interview patients on their past medical history and highlight their perspective of the treatment they were receiving in the hospital. Also, I anticipated studying and observing a number of patients closely, so I would be able to track their daily progress. With these findings, I would be able to construct thorough research of how doctors at RVTH handle and treat patients with liver cancer.

Methodology

A normal work day at RVTH

I began working in the Internal Medicine male ward at RVTH on February 8, 2011. I dedicated 8-10 hours a week, visiting the site on Tuesday and Wednesday for 4-5 hours a day. On site, I would frequent the Accidental and Emergency and Infectious Disease department in search of doctors caring for patients with liver cancer. When there were no patients in the ward that were suspected of or exhibited liver complications, I consulted doctors from other wards. Through this method I would generate a larger sample for patient information. I exhausted all possibilities of seeking liver cancer patients. Aside from information gathered from observation, I visited the record keeping department to collect written information. I compared both patient records and personal observations as the source of information for this research project.

An average day within the Internal Medicine ward would start with “ward rounds.” This consists of the head doctors and nurses checking the progress and vital signs of every patient. During this time, I would engage in a discussion about the patient’s diagnosis, progress/regression and treatment. I took advantage of this opportunity to gather information because doctors were most willing to speak on a specific topic related to the patient’s condition. If there was any additional documentation the doctor needed to analyze or review such as CT scan, x-rays and ultrasound results, I joined and observed the readings. When necessary, if a patient required more attention

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such as a feeding tube needing to be inserted, cleaning and dressing wounds, or performing intravenous injections, the nurse would handle all of these tasks. Once ward rounds are completed, patients are administered their medicines and are then looked after for the day. I generally relocated to either the record keeping department or to the accident and emergency (A&E). There I encountered an overwhelmingly busy and chaotic environment. The change of pace offered the opportunity to identify any patients suspected of liver complications because all patients are seen in A&E before they are admitted into a particular ward. I was more assistance in this department because I helped record basic information about the patient while shadowing a doctor handling a patient. I was given permission to perform minor tasks such as assessing patients' motor and memory skills, measuring blood pressure and respiratory rates. I also documented any gross physical abnormalities observed.

Developing a focus

Upon my arrival to The Gambia, I wanted to investigate the major causes of death aside from malaria and HIV/AIDS. I discovered over \$1.5 million in funding was received from the Global health Research Initiative for a four year period to support research in HIV/AIDS and nearly \$168 million was donated to fight malaria from The Bill and Belinda Gates Foundation (Gates 2008). Though research efforts to control the spread of HIV/AIDS and reduce the contraction of malaria are exceptionally commendable, these diseases have gained global recognition and support whereas the awareness of cancer in The Gambia is not as prevalent. There has been a lot of effort to make people in the community more aware about HIV/AIDS and malaria, but there is little information about the Hepatitis B virus, which is easily transmissible and preventable. Therefore, I wanted to base my research on a disease that is common to The Gambia and was not receiving much research effort within the past several years.

After visiting the UK's Medical Research Council in The Gambia (MRC) website (<http://www.mrc.gm>), I noticed the extensive research and work that has been conducted over the past decade concerning the hepatitis B virus and vaccinations. For personal and academic reasons, I sought this as an opportunity to contribute my research efforts in this ground-breaking study. My desire to research the relationship between hepatitis B vaccinations and end-stage liver disease quickly turned into the desire to study a similar, but different topic. After consulting Dr. Ousman Nyan, chief medical director of RVTH, he suggested that I focus on something more feasible – something that I would be able to research while working at RVTH. Time was presented as the most difficult challenge because in order to research such a topic I needed more than just 4 months. The difficulty in gathering information about individuals that participated in the hepatitis B vaccination study years ago was far more than I was willing to explore given my circumstance. It would require extensive research and experience.

As a result, I modified my topic to “hepatitis B in The Gambia.” By this time, I had started working at RVTH. And within the short weeks of working there, I realized that it would be difficult to conduct direct research about this topic. In search of a new institution where I could possibly carry out my research, I contacted Dr. Kalifa Bojang, a prestigious doctor working at MRC that contributed to the research in the hepatitis B virus vaccinations. Prior to our meeting, I devised a new plan of research “the effect of aflatoxin on the development of hepatocellular carcinoma in hepatitis B patients.” Yet again, I was advised to change my topic because it required access to a lab, funding for research and time. Determined to settle on a research topic that was feasible I changed my topic to “the effect of hepatitis B on the development of liver cancer.” Given my place of work, I would not have access to the laboratory resources necessary to develop legitimate findings. Eager to finalize my topic, I consulted doctors and medical students working at RVTH for

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suggestions. I was able to generate the basis of my topic from several of their suggestions; a topic that would be feasible to conduct at RVTH. I would have means to conduct research about the clinical treatment of HCC in The Gambia through interviewing doctors about their personal experience with treating patients and by access to patient records.

As a means to collect information about clinical treatment in The Gambia, I researched online resources and literature and was unable to obtain sufficient information. Therefore, I consulted the best source about clinical treatment - the doctors who treat HCC patients. I conducted interviews with several doctors working in the Internal Medicine, A& E and pediatrics department of RVTH. I asked a series of questions about the symptoms that patients exhibit, the stage of cancer, initial protocol and the tests that are conducted at the hospital. More importantly, I wanted to highlight the measures taken to accommodate a patient with HCC. I also took note of any challenges or difficulties encountered when treating an HCC patient – palliative care and/or referral to another location better equipped to treat patients. These interview data would be used to form an in depth personal view of clinical treatment of an HCC patient in The Gambia. In addition, patient records were used to collect detailed information such as the age and gender, specific diagnosis, admission and date of death (if applicable). This information would validate whether patients selected for this research were indeed suffering from HCC or liver related complications.

In order to find more information about the high incidence of HCC in The Gambia, I not only researched and used literature, but the opinions, knowledge and concerns of average Gambians within the society. I interviewed several people who I had established a relationship with in the short time of being in The Gambia. The interview focused on traditional medicine and its significance, and cultural beliefs about sickness. This information would provide a clearer understanding of why so many individuals that suffer from HCC seek clinical medicine when the

chance for survival is too late. I specifically interviewed Ababoukarr Sillah, head of the National Traditional medicine unit, in order to obtain accurate information about the diagnostic tools and procedures employed by traditional healers for individuals that consult them for liver cancer.

Relevant Literature

In order to compensate for the time spent devising a viable research topic that took into account the constraints I had in terms of money, access to a laboratory, and other resource considerations, it was imperative that I started collecting information immediately. Although, my initial research topic was related to my finalized topic, I still needed to gather more information. I referred to several online articles concerning the main causes of HCC, the manifestation of the illness and any general statistical data. In the online article entitled *Hepatocellular Carcinoma in The Gambia and the role of Hepatitis B and Hepatitis C*, researchers Clement Mbotto, Angela Davies-Russell, Mark Fielder and Andrew Jewell conducted a study on 13 patients with a proven history of HCC and 39 healthy controls. Each patient was screened for both hepatitis B surface antigen (HbsAg), a marker that indicates current hepatitis B infection, and for the anti-hepatitis C virus (anti-HCV), (i.e. a test that detects the presence of antibodies unique to the Hepatitis C virus). Therefore if an individual generated a positive result for HbsAg s/he was infected with the HBV. Likewise, if an individual possessed antibodies specific to the HCV then s/he was infected with the HCV. Their results stated that HbsAg was detected in 38.5% (5/13) and anti-HCV was identified in 7.7 % (1/39) of persons with a history of HCC. Rates for each type of viral infection were higher in men than women. Their results indicate the co-existence of both HBV and HCV as non-contributing factors to the development of HCC, but rather the independence of HBV as a cause for HCC. Finding suggested that 50% of HCC cases may be due to non-viral factors and calls for further

research into determining the causes. This article provided insight on the influential effects of HBV and HCV on the development of HCC in The Gambia (Mbotto et al 2005).

In the second on-line article entitled *Molecular epidemiology of human liver cancer: insight into etiology, pathogenesis and prevention from The Gambia, West Africa*, authors Gregory Kirk, Ebrima Bah and Ruggero Montesano investigate the independent and combined effects of HBV, HCV and dietary aflatoxin (i.e. a toxic compound that grows on moldy grains and nuts) exposure on HCC. Through a series of case controlled studies, population surveys and field trials, the natural history and pattern of the Gambian population was defined. Their results suggest the high incidence of HCC as a consequence of childhood HBV, lifetime dietary aflatoxin exposure and chronic HCV infection. In the Gambia, ~57 % and ~20% of HCC cases are attributable to chronic HBV infection and HCV infection, respectively (Gregory 2006). In a third online article entitled *Aflatoxin exposure and viral Hepatitis in the etiology of liver cirrhosis in the Gambia, West Africa* Mark H. Kuniholm et al. examine the association between environmental and infectious exposure and cirrhosis of the liver in The Gambia. Ninety-seven individuals were diagnosed with cirrhosis using a validated ultrasound scoring system and were compared with 397 controls. Participants reported demographic and food frequency information. Candidates were tested for HBV, HCV and aflatoxin mutation (Kuniholm et al 2008). Acute levels of aflatoxin (aflatoxicosis) were found to have a significant increase in the risk of cirrhosis. Also, aflatoxin exposure and chronic HBV infection may interact synergistically to increase the risk of liver cirrhosis. Approximately 58.8% of cirrhosis cases were positive for the hepatitis B surface antigen, which is indicative of the virus. More than half (54%) of the cirrhosis participants in the study were moderate consumers of groundnuts during his/her lifetime, which suggests the impact.

Findings & Results

Part One: Introduction

Trend of Hepatocellular Cancer in The Gambia

The Gambian National Cancer Registry has recorded a total of 2975 cases of liver cancer for 2179 males and 796 females from 1988 to 2006 (Hall 1987). The incidence data gathered from over the first 10 years of registration (1988-1997) and the most recent data (1998-2006) suggest an overall increase in liver cancer diagnosis in The Gambia. More specifically, HCC was found to be the most frequent cancer, representing 62% and 28% of men and women respectively of all cancer cases recorded in the Gambia National Cancer Registry (Sighoko 2011). The more recent study suggests an increase of liver cancer among females and a stable trend among men. A recent study of 323 clinically assessed cases from the Gambia showed that over 90% of the cases presented with very advanced liver cancer.

Hepatocellular carcinoma: Hepatocellular cancer

Hepatocellular carcinoma is a cancerous tumor composed of cells that are similar to hepatocytes, liver cells that secrete bile. Hepatocytes compose 80% of the liver tissue; and over 90% of liver cancers arise from these liver cells (Stuart 2010). HCC can either originate as a single tumor that grows larger or in multiple tumors. It is not until the latter stages of cancer, when the single tumor spreads to other surrounding organs, that metastasis HCC occurs. The second type of HCC originates as many small nodules throughout the liver, rather than just a single tumor. This is a result of liver cirrhosis or chronic liver damage.

Cirrhosis of the liver is a condition that causes the liver to slowly deteriorate and malfunction due to chronic injury. As a result, scar tissue substitutes for healthy liver tissue, thus causing a partial blockage of blood flow through the liver. Unlike a healthy liver that is able to

regenerate its own cells, a liver in the end-stages can no longer effectively replace damaged cells. Consequently, this impairs the ability to control infection, remove toxins from the blood, process nutrients, hormones and drugs, and make proteins that regulate blood clotting. It also impairs the liver's production of bile (i.e., a secretion that helps absorb fats including cholesterol). Without proper liver function a person may experience liver failure and ultimately death (Wolf 2011).

Part two: Main causes of Hepatocellular Cancer in The Gambia

Hepatitis B virus (HBV)

Natural History

Chronic HBV infection is endemic in The Gambia, therefore a high incidence of carriers exists in the population. Unlike the common forms of transmission such as piercing, intravenous drug-use, sexual penetration and mother-to-child transfer in Western and Asian countries respectively, most HBV infections in The Gambia are a result of horizontal transmission, the spread of an infectious agent from one person or group to another, occurring during young childhood. Although the exact methods of transmission are unclear, the risk for Gambian children is increased with an older sibling or mother who is an HBV carrier and the presence of a non-healing skin condition (Kirk 2006). Likewise, in the African country, Ghana, household transmission was identified as the primary setting for HBV transmission. HBV transmission is highly dependent on the infectivity of the carrier. Mothers are more likely to transmit HBV to her children during active replication. As a result, the children will be chronically infected. When the virus is actively replicating, (i.e., hepatitis B viral particles penetrate the carrier's DNA and as DNA replicates the virus replicates) the transmission of the virus is more likely to occur rather than when the virus is in an inactive state of replication (Kirk 2006). In other words, when the hepatitis B viral particles are not replicating they are dormant. Among Gambian chronic carriers, the prevalence of HBV DNA

detection declined with increasing age after adolescence, with almost no active replication of the virus after the individual passes 25 years of age. In comparison to Asian countries, there is a notable difference among populations. In Asian populations active replication often persists into advanced age (Kirk 2006).

The effect of the HBV in Gambians may be attributed to unique genetic characteristics and the geographical significance of HBV genotypes. In most African countries, the distribution genotypes are commonly A, D or E, while Asian countries are commonly genotypes B or C. There is increasing evidence of different genotypes resulting in different clinical outcomes (Kirk 2006).

What is Hepatitis B and its effect on the development of HCC

Hepatitis B is an infection of the liver caused by the hepatitis B virus (HBV). The hepatitis B viral particles penetrate the liver cells, hepatocytes, transporting their components into an individual's deoxyribonucleic acid (DNA). The structure of the HBV consists of a core particle (central portion), which is composed of DNA and a core antigen (HBcAg), and the surrounding envelope (outer coat) contains the surface antigen (HBsAg). HBsAg carries distinctive markers that are identified by artificial hepatitis antibodies (Vierling 2007). This is an essential test to determine the diagnosis and evaluation of patients that are suspected of viral hepatitis.

HBV reproduces in the liver, but does not cause direct damage to the liver itself. Instead, the presence of the virus causes an immune response that ultimately results in the body eliminating the virus so the liver is able to recover. This process induces inflammation, thus resulting in severe damage to the liver cells. Generally, healthy individuals that contract an acute HBV infection resolve all clinical symptoms and are able to maintain a lifelong protective immunity to HBcAg and HBsAg. However, an individual that is unable to combat the virus suffers the devastating effects it

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has on the liver. Over time, the virus will mount an immune response causing the hepaocytes to be targeted and damaged. This on-going process will cause the increase of scar tissue replacing the healthy liver cells. As a result, the scarring of the liver will evolve into hepatocellular carcinoma.

In order to determine the effect of the hepatitis B virus infection on hepatoma carcinoma, I referred to a study that carried-out a case-control investigation of 70 persons with hepatoma and 70 controls and their families selected and studied between 1981-1982 in The Gambia, West Africa. Hepatoma occurred more than twice as frequently among persons who had four or older siblings as compared to persons who had less than two older siblings. This suggests the high incidence of hepatitis B virus in The Gambia and the influence it has on the number of individuals that develop HCC (Ryder 1992).

Dietary Aflatoxin consumption

Natural History

The majority of HCC in Africa and more specifically in The Gambia is attributed to HBV and HCV, however the influence of aflatoxin on hepatocarcinogenesis (i.e., the production of cancer in the liver) is a major contributing factor to HCC. Aflatoxins are toxic and carcinogenic metabolites of molds (i.e., cancer causing products made from the metabolic process of molds). Aflatoxin found in The Gambia is produced by the species *Aspergillus flavus* and *parasiticum*. This particular aflatoxin contaminates a variety agronomic crops, particularly groundnuts (or peanuts), maize and cottonseed, in countries with hot and humid climates. In The Gambia, groundnuts are cultivated as both a staple food and primary cash crop (Wild 2000). Aflatoxin B1 (AFB1) is the main metabolite produced by these particular molds (Kirk 2006). As a result, the consumption of these aforementioned agricultural commodities results in high and prolonged exposure to AFB1. Studies have shown a clear relationship between the exposures to AFB1 contaminated foods and the

risk of HCC in Sub-Saharan Africa and Southeast Asia. However, these studies did not expound on the causal association of dietary exposure to AFB1 and the effect of HCC due to poor assessment and minimal resources concerning the independent effect of the HBV on HCC (Kirk 2006).

Specifically in The Gambia, recent studies have shown AFB1 as a contaminant in many local food dishes because of the exposure to contaminated groundnuts. Consequently, the frequent consumption of groundnuts in the population suggests high levels of exposure are present in almost all Gambians. More commonly among Gambians, exposure to aflatoxin occurs during the entire lifespan, starting at the birth. When the mother is bearing the child and when she gives birth are the probable modes for transferring the aflatoxin-albumin compound to the child (Wild 2000).

Generally, rural Gambians exhibit higher levels of AFB1 compounds than urban residents. This suggests there is a higher consumption of groundnuts in rural areas than in urban areas where there is a more diversified diet (i.e., access to a larger variety of food types). Also, the strong correlation between exposure to AFB1 and seasonal variation, implies the availability of groundnuts and the consumption of AFB1 are directly related. The prevalence and quantitative levels of AFB1 exposure in The Gambia are among the highest in the world. Therefore, Gambians are most susceptible to acquire complications that arise from consuming aflatoxins found in groundnuts (Wild 2000).

How Aflatoxin affects the liver

AFB1 is the most potent type of aflatoxin. Aflatoxins interfere with normal processes of DNA and RNA synthesis, which in turn limits the production of proteins in the liver. The toxin is able to penetrate between DNA molecules and induce a mutation that affects the liver. As a result, this interference causes inflammation and hemorrhage. It has a negative impact on the immune system because it interferes with the normal pathways and drastically reduces the number of

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antibodies made to fight off infection. Two main effects of aflatoxins can cause acute or chronic aflatoxicosis. In acute aflatoxicosis, an acute hepatic necrosis develops which can later evolve into cirrhosis or in more severe cases, liver carcinoma. In most cases, if an individual has acute aflatoxicosis the end result is death. When an individual is suffering from chronic aflatoxicosis, the symptoms are not as severe as acute aflatoxicosis. However, the immune system is suppressed and the possibility of cancer developing is probable.

Part three: Influences that contribute to HCC

Lack of awareness and promotion of liver cancer

Although intense research has been conducted focusing on the Hepatitis B virus in the Gambia by researchers at the Medical Research Council (UK) in The Gambia, consequences of hepatitis B virus and the effects of aflatoxins on the development of liver cancer are still prevalent. As part of the Extended Programme of Immunisation, 60,000 children were administered the hepatitis B vaccine; nearly 20 years later the vaccination appears to have been very effective. Approximately 84% of people who were vaccinated, 94% were protected from becoming chronic HB carries (Inskip 1991). These findings were promising results for future generations. However, approximately 50% of male liver cancer deaths are attributed to the hepatitis B infection. In order to make an impact, prevention is the key for change in The Gambia. The effort in establishing the vaccination program in the Gambia is ground-breaking and promising, but there are other methods of reducing the transmission and subsequent contraction of the virus.

After speaking with several doctors working at RVTH, I sought their opinions and knowledge of hepatitis B control and liver cancer awareness within the community. To maintain anonymity, I will not reveal the speaker. He suggested that most of the funding and attention was focused on malaria and HIV/AIDS, instead of liver cancer. Through personal observation, there is a

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diversion of attention with the hepatitis B vaccination. There seems to be a relapse in the number of individuals that are infected with the virus. Through online research and consulting with doctors within the Greater Banjul area, there are hardly any prevention programs that aim to reduce the spread of hepatitis B virus. I have noticed posters and flyer advertisements concerning HIV/AIDs, malaria and tuberculosis, but I have yet to witness a sign informing people in the community about liver cancer and the HBV.

Consequently, the lack of public awareness about the hepatitis B virus perpetuates the issue of people not understanding the virus, transmission, symptoms and its effects on the body. When there is no public prevention implemented this increases the chances for transmission and infection. Whereas, if the community is exposed to information about HBV and programs were held that generated awareness, ultimately it would reduce the transmission rate. Likewise, information about aflatoxin is rarely spoken about. By simply drawing attention to the adverse effects of eating molded groundnuts, people may change their habits and adhere to the recommendations provided.

Traditional Medicine

I was granted the opportunity to interview the director of the National Traditional Medicine Program about traditional medicine and its significance in the Gambian society. Upon consulting the director I learned that traditional medicine is an integral part of Gambian culture. This insight was reinforced by engaging in casual conversations with Gambians with whom I have established a relationship. The influence of traditional medicine on people's ideas about health remains strong. By utilizing the medicines prescribed by the traditional healer as therapeutic relief and treatment, it can either serve as a healing supplement or, in many cases, as a harmful agent that worsens the individual's condition. Hence, I wanted to explore the reasons why most individuals, in addition to the aforementioned viral and dietary causes of liver cancer, when admitted to hospital are in the

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most severe stages of liver cancer. I assumed that individuals consciously suffering from liver cancer would consult a traditional healer just for treatment in some cases more so than seeking clinical attention, so I discussed the topic of how a traditional healer treats an individual suffering from HCC with the director to gain a clearer understanding of traditional medicine's influence and effect suffering. In order to maintain anonymity, I will not reveal the name of the speaker.

Traditional Medicine Overview

According to our discussion, the use of traditional medicine began long ago and has continued for many years. Gambians use a variety of herbs, plants and roots in ways very similar to what their ancestors used as healing agents. Humans possess a cardinal principle for survival and therefore the knowledge and practices associated with the use of plants and other items to promote human health is cultural. It is a way of learning and utilizing the accessible items to facilitate well-being or the healing of people who become ill. Traditional medicine has been around much longer than what we know today as conventional scientifically-based medicine. As time progressed, the nature of these folk remedies maintained its basic therapeutic effect, but preparation and technique has changed. These natural remedies were passed down from generation to generation through written and oral documentation. Therefore, the existence of traditional medicine in the Gambian culture has long been established as a legitimate source of healing and treating sickness.

Traditional Medicine: Treating Liver cancer

Since the majority of Gambians consult a traditional healer at some point during their search for therapeutic relief, I was curious to know if there were any specific treatments or therapies for liver cancer. The speaker explained the process of diagnosis and treatment for someone suffering from liver cancer. In some cases, the traditional healer would either communicate with *spirits* or through a medium to a higher being to assist in assessing the individual, if the condition was

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unknown. Also, the traditional healer would devise fortune telling means or water gazing methods to ascertain the type of illness the person is suffering from. Healers also acquired this knowledge through apprenticeship, experimentation and observation – in addition to this empirical local knowledge, the power of prayer and use of the Holy Koran. The person is either clinically diagnosed with liver cancer or unaware of their condition. In the instance of a person who is certain s/he has liver cancer, it claims have been reported of traditional healers curing the cancer, but the alleged cure has not been verified due to the healer's refusal to share his/her treatment efforts. In cases where complications of the liver are probable, the traditional healer conducts an external physical exam to feel the size and texture of the liver. In addition to diagnosing the individual, the past history and current symptoms are recorded. For internal ailments it is difficult to diagnosis. Nonetheless, healers use their experience and observations to perceive what the individual is suffering from. Generally, persons that are suspected of liver cancer would complain of abdominal pains and may exhibit an enlarged abdomen. For abdominal pains aside from stomachache, the traditional healer would prescribe an herb or plant leaf that would induce vomiting and diarrhea. The exact name of the plant is unknown to the healer and to the person using the medicine. In most cases, the plant name is labeled in the local languages, but is not able to be translated in English. As a result, neither healers nor those treated by the traditional healer is able to perform a research analysis of the plant. The lack of standardization and degree of toxicity of traditional medicines presents the potential issue of causing the individual more harm. There are cases when individuals who consult traditional healers mix several herbs together in the event that one herb is ineffective. This also can have grave consequences and in many cases even more detriment to the liver.

The influence on liver cancer

In many cases, people that suffer from liver cancer either consult traditional healers and use traditional medicine before seeking conventional medicine, or seek conventional medicine and believe the effort of treatment is not effective and consult the traditional healer. In order to gather additional information I interviewed doctors who had documented the medical history of the liver cancer patients they treated. Although information was obtained, the information lacked specific details. The majority of liver cancer patients that are seen at the RVTH are in the end-stages of cancer because traditional medicine is their first option whilst conventional medicine is their last resort. During this prolonged time without clinical attention, the cancer steadily deteriorates the natural function of the liver. The addition of toxic herbs and plants that induce vomiting and diarrhea put more strain on the liver causing the liver to fail at a rapid pace. Because the liver's natural function to filter toxins and excess proteins is impaired significantly, the exposure to lethal toxins presumably destroys the remaining healthy parts of the liver, if any. Individuals that consult conventional medicine first before seeking the traditional healer, in some cases, believe that the treatment prescribed by doctors is ineffective if they experience pain. The issue in trying to convince or educate the patient in terms of treatment and effectiveness can present a problem. Generally, when a patient is stable and s/he is discharged they will revert to using traditional medicine in hopes of curing their disease.

Part four: Clinical treatment of HCC at RVTH

Findings at RVTH

While working at RVTH, I was able to record the number of cancer patients, dead or alive, seen at the hospital over a two month period. Within the last two months RVTH has seen 106 cancer patients, 34 of them being liver cancer patients. Figure1 illustrates the total number and type

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of liver cancers. Among the 34 patients, 17 of the patients were diagnosed with hepatocellular carcinoma, which is majority of the patients. These findings suggest that HCC is the most common liver cancer seen in patients at RVTH. As previous studies have shown, HCC is more common among men than women. Figure 2 supports previous findings by illustrating the greater number of men that were diagnosed with HCC than women.

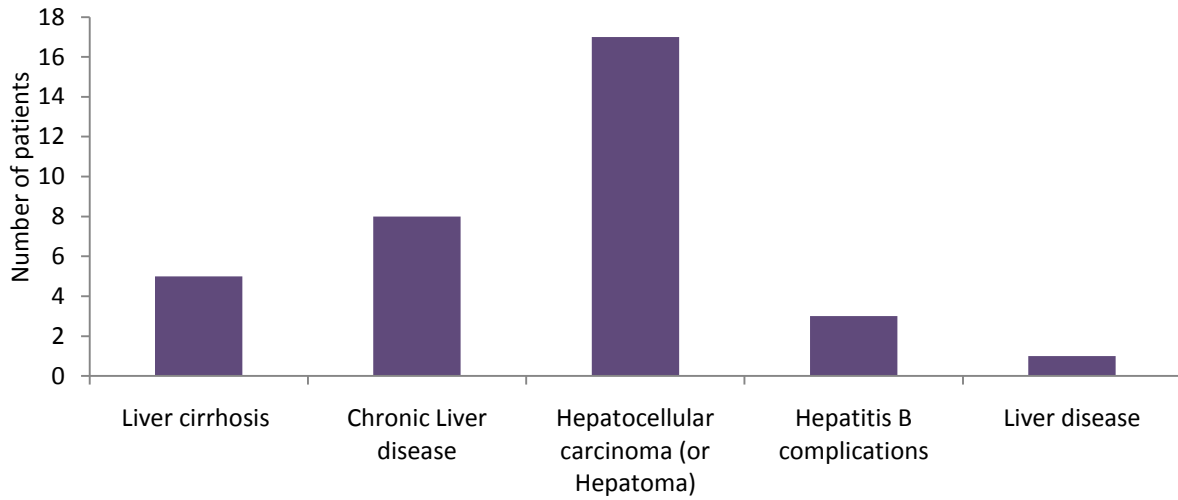


Figure 1. Number of male and female patients seen at Royal Victoria Teaching Hospital(RVTH) that exhibited either liver cirrhosis, chronic liver disease, hepatocellular carcinoma (or hepatoma),

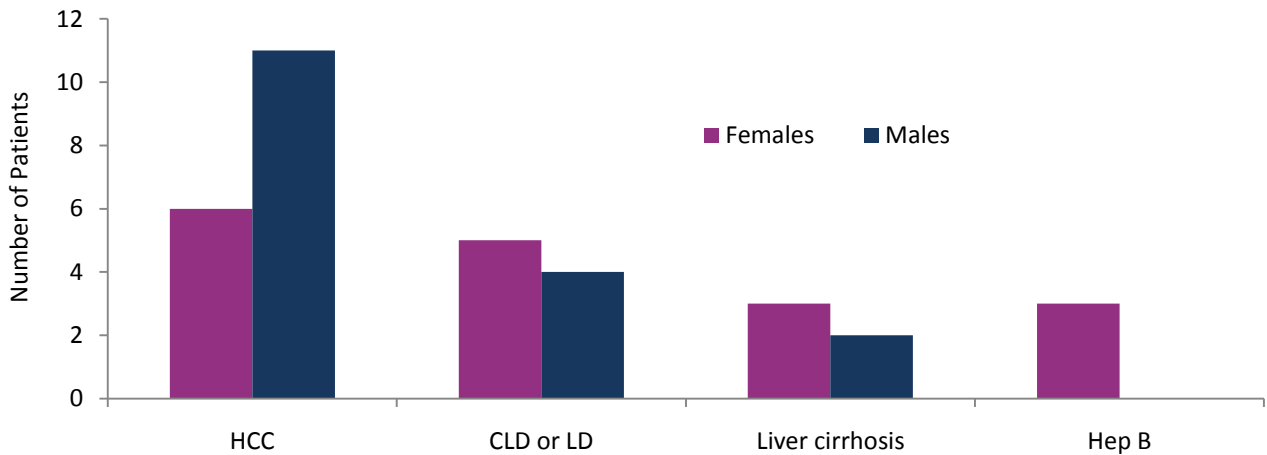


Figure 2. Comparison of male and female patients seen at Royal Victoria Teaching Hospital (RVTH) that have been diagnosed with HCC, chronic liver disease(CLD) or liver disease(LD), liver cirrhosis and Hepatitis B virus (HBV)

General Protocol

In order to effectively gather information concerning clinical treatment of HCC, I needed to consult the doctors who treated the HCC patients. Generally, when patients are admitted to RVTH they are near the end, most severe stages of HCC due to the influences and causes that were previously stated. In the effort for doctors to treat these patients a series of procedures must be met to ensure proper care. I referred to patient records and conducted several interviews with Dr. Bully Camara, Dr. Baboucarr Sanyang and Mr. Lamin Giana in order to produce a general scope of clinical treatment. For privacy purposes, the name and information provided will not be associated in of any patients.

Vital Signs and Laboratory Tests

Before treating the patient the vital signs and symptoms must be identified. In cases of HCC, the blood pressure (BP) is usually low due to shock depending on the stage of cancer. The respiratory rate may be tachypnoeic (fast respiration) due to ascites (i.e., swelling of the abdominal cavity due to a build-up of fluid). Generally, patients exhibit signs of abdominal pain, abdominal swelling, jaundice (yellowish hue to the white part of the eye) and darkened urine. As well as anorexia, occasional swelling and non-specific symptoms like the feeling of not digesting properly. After the symptoms are assessed, in order to confirm or establish a diagnosis laboratory tests need to be performed. Most commonly when a patient is suspected of liver complications or liver cancer a series of tests are requested. If the hepatitis B surface antigen test results show positive then the patient is infected with the virus and likely to be actively replicating the hepatitis B virus. The alpha fetoprotein (AFP) test, checks the level of AFP being produced. If production of AFP is low then this is suggestive of liver abnormalities. In addition, the function of the liver must be assessed in order to confirm diagnosis and potential treatment for the patient.

Biochemistry	Patient results	Reference Range
Albumin	25 g/L	35-55 g/L
ALP (Alkaline Phosphate)	173 μ /L	35-129 μ /L
Alanine Aminotrans	33 μ /L	0-43 μ /L
Aspartate Aminotrans	191 μ /L	0-42 μ /L
Bilirubin direct	15 μ mol/L	0.0-3.4 μ mol/L
Bilirubin total	35.5 μ mol/L	1.0-20.0 μ mol/L
Creatin	44 μ mol/L	60.0-80.0
Total protein	61.0 μ g/L	53-97 μ mol/L

Table 1. Biochemistry results of an anonymous patient diagnosed with hepatocellular carcinoma at RVTH.

Generally in hepatocellular carcinoma patients, the bilirubin levels are higher than normal because the liver has decreased filtering capabilities. Table 1 shows the patient's results for both bilirubin direct (the level of bilirubin within the liver) and bilirubin total (the total amount of bilirubin in the body) is much higher than the normal range. Also, the patient exhibits high levels of ALP which is suggestive of build-up in the liver. I used this particular patient's information to illustrate differences of biochemistry levels in a normal patient and a patient suffering from HCC. I gathered this information from the record keeping department in RVTH.

A Doctor's Insight: Treatment

When the results for a patient are confirmed for HCC, the doctor will begin palliative treatment. Palliative treatment is the effort to maintain comfort and care for a patient with a terminal illness. At this point, making sure the patient is physically and emotionally comfortable is a priority. In cases where an HCC patient is suffering from ascites, infections or fevers then drugs and medicines will be prescribed accordingly. Normally in all HCC cases, pain killers and vitamins are prescribed when necessary if patients are admitted into the ward and under the care of a doctor. HCC patients are sensitive to anything potent if consumed because their liver's ability to filter is impaired. Tramadol and diclofenac are two common pain killers administered to HCC patients through intravenous injection (through a vein in the body) for pain and discomfort. The dosage and

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frequency of the drug given depends on the severity and how often the patient experiences discomfort. After reviewing records and consulting several doctors, a common dosage for tramadol and diclofenac are 50 mg and 75 mg respectively. For HCC patients, experiencing severe pain morphine, petidine and BF-118 are given to the patient. In most cases, these drugs are not readily available so doctors prescribe what is available.

Most cases of HCC patients do not live long once admitted to RVTH. They usually die within 24 - 48 hours. Of those that survive longer than 48 hours the life expectancy may extend to a few months. Patients in such a severely degenerated condition are those that have exhausted all possible options for treatment, mostly consulting traditional healers, before seeking clinical medicine. At this point, the patient is near death.

In spite of a challenge

When patients exhibit an acute sign of HCC the possibility to perform chemotherapy is unlikely because there are no resources to do so at the hospital. Therefore, patients are labeled as out-patients and are sent home on a medicine regime. They are to check in with the doctor to confirm their progress and alert the doctor of any sudden changes of their condition. Early stage patients have the option of going to Dakar, Senegal for chemotherapy and treatment, but such procedures are very expensive and unaffordable to most patients who come to RVTH. Even those in

Liver Complication	Out-patient	In-ward death	Discharged	In-ward
Liver cirrhosis	3	2	0	0
Chronic Liver disease	3	2	2	1
Hepatocellular carcinoma (or Hepatoma)	10	4	0	3
Hepatitis B complications	0	2	1	0
Liver disease	0	0	0	1
Total	16	10	3	5

Table 2. Status of liver cirrhosis, chronic liver disease, HCC or Hepatoma, Hepatitis B complications and liver disease patients seen at Royal Victoria Teaching Hospital (RVTH) of a two month period.

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the early-stages of cancer that have a chance for survival are unable to take advantage of the possible benefits from the treatment in Dakar because of financial reasons. So they revert to traditional medicine as a means to cure or treat the illness, but however it complicates the illness more. Table 2 shows the number of out-patients, in-ward, death in-ward and discharged HCC patients at RVTH.

As the table depicts, most patients with liver complication are out-patients. The doctor will send the patient home if they have stable vital signs and exhibit no form of distress. In order to maintain an equal ratio of hospital beds to patients, doctors must determine which patients to admit and which patients to discharge. The doctor will prescribe pain killers and multi-vitamins for the patient to take. Although, they are suffering from a terminal illness, there is not much that can be done to prolong the life of the patient. They will follow the natural course of life. The small percentage of HCC patients that are in-ward are in the worst conditions and need alleviation of their symptoms and suffering.

In the effort of diagnosing and treating in-ward patients, doctors encounter many problems. Generally, after 2 o'clock in the afternoon the laboratory is not open and tests are not available. Thus, the common liver related tests (e.g. surface antigen, alpha fetoprotein, liver function, among others) cannot be executed. If a doctor has an urgent need for the results to a test, s/he must wait until the next day or until a lab technician is available. This can ultimately increase the chances of the patient dying because treatment is unable to begin without confirming the condition of the patient. At times, tests can usually take up to 2-3 days before the doctor is able to receive the results because for particular tests it is expensive to run and lab technicians must gather multiple samples.

In addition to issues with gathering test results, there is a lack of specialty care in The Gambia, specifically at RVTH. When medical students train at RVTH and become doctors a high

percentage of them practice abroad(<http://africanpress.wordpress.com/2008/12/13/gambian-doctors-leave-their-country-and-their-people-for-better-opportunities-abroad-being-selfish/>) So the need for foreign doctors is apparent. The language barrier and cross-cultural differences, not only create problems with the patients, but with the other doctors as well. There is a lack of highly-trained physicians to operate the lab equipment. So the issue of having certain tests done is a major problem. In many cases, either the equipment malfunctions or it is broken. Since patient records and information are manually scripted, illegible handwriting and language is an issue. The process of transferring information from one document to the next presents the opportunity for mistakes and errors as well.

Discussion

The information and data I gathered for this project are significant and important to the well-being of the Gambian society. The purpose of my research is to highlight the main causes and contributing factors of HCC, as well as the effectiveness and quality of clinical treatment for HCC. My findings can generate awareness about how to minimize the possibilities of developing HCC in The Gambia only if this is used to create an awareness program for the Gambian public. In some cases, the development of HCC is attributed to genetic reasons, but for majority of individuals that develop HCC, is due to previously stated reasons. Therefore, my research efforts in emphasizing how HCC is caused and the common route individuals choose to take makes all the difference in their likelihood for survival. Since the incidence rate for HCC is alarmingly high, I hope this research would contribute in informing the community and relatives of patients admitted to the hospital about how preventable HCC can be. Aside from contributing factors on the development of HCC, once diagnosed the chances of receiving effective clinical treatment for the terminal illness is limited. In many ways HCC is preventable, by taking the preventative measures (i.e. maintaining

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good hygiene, a healthy diet and getting vaccinated) the probability of developing HCC is unlikely.

And those who are fortunate to identify the cancer in the early stages may be able to receive effective clinical treatment rather than seeking medical attention at the end stages. Although, there is no chemotherapy for liver cancer, there are other alternatives to receive effective treatment.

RVTH can use my research findings to create awareness and educate the relatives of patients that are seen at the hospital. It may also bring awareness to in-training nurses and medical students about how to care for and treat a person suffering from HCC. Since the patient's comfort and well-being at the end stages of life is very important, it is imperative that medical staff are aware of their interaction with the patients. It will highlight the importance of the need for care in the hospital.

Despite the constraints that inhibit doctors from clinically treating patients, they utilize the resources available to effectively treat their patients. In researching HCC in The Gambia, I believe my objective for generating a successful study was achieved. Although I encountered several problems at the start of my study, such as ascertaining a relevant source for collective data for all liver cancer patients admitted to RVTH. I was later directed and introduced to several medical staff that could supply with this information. By talking and handling patients, I gained a sense of confidence with my language abilities and enhanced my communication skills.

For the majority of my time working at RVTH, I was surrounded by terminally ill patients near death. Working in such an environment presented the emotional and mental challenge of maintaining composure and poise in the eye of the patients and doctors. Because I was bounded by sympathy and grief for patients, I perceived the hospital environment as dismal. I experienced on numerous occasions, interacting with patients that were stable one day and dead the next. The feeling of knowing that death is a common occurrence inside the walls of the ward was far too

much to bear when I first arrived. I had never seen dead or near dead bodies, so the experience was emotionally impactful. Eventually, death although reoccurring was still common, I grew tolerant.

RVTH was a place where I learned about my research topic and other common medical conditions in The Gambia. I developed a research plan, searched for various resources and methods, gathered information and presented my findings. I believe a successful research project requires a detailed plan. First, outlining your ideas and steps in ascertaining information about the topic and secondly, devising a solid research topic and plan of execution.

I plan on sharing my research paper with doctors who I shadowed at RVTH. I will print out several copies and email copies to them and other doctors who assisted me in my day-to-day activities.

Next Steps

My experience

My experience working at RVTH has furthered the processes that have shaped me into a well-rounded student and person. In any environment where you are challenged to withstand physical, mental and emotional distress, the likelihood of learning and viewing things in a different light is probable. The environment was conducive for learning and conducting research. The hospital experience in The Gambia is quite different from experiences I have had in the USA.

From the minor examinations to the ailing patients, I have grown to understand the natural course of life and how clinical medicine is able to, in many ways, intervene and change the outcome. From this experience, I have gained clinical experience and I am now more knowledgeable about the Gambian hospital environment. Since I plan to become a medical researcher, having the opportunity to assist in analyzing patient symptoms, tests and screenings and freely question doctors about any questions that I may have is a great experience. I gained a better

understanding about the clinical manifestation of an illness, disease and/or infection and learned the steps in assessing and applying my knowledge.

PEACE Program Suggestions

I would certainly recommend RVTH as a service-learning/directed research site because it is an excellent environment for inexperienced prospective medical students and/or novice medical researchers. Since it has become a “teaching” hospital, they encourage learning and applying medicine through hands-on interaction with patients. The doctors are friendly and are willing to assist in your research efforts. They are enthusiastic about involving you in examinations, data analysis and treatment protocols because they support any research that is being conducted at RVTH.

Students planning to conduct research at RVTH should propose a topic that directly deals with observations and collecting data working at the hospital (i.e., interviewing doctors, talking with patients, recording patient conditions) rather than a topic that requires any lab work. The main component to a successful research project is feasibility. Understanding the conditions of work prior to creating a topic is ideal because the topic and your work site may not be compatible. Also, planning is an essential part of creating a successful project. When you plan ahead you give yourself more time to make changes and/or refine your topic. I encountered issues with choosing a particular topic, but did not experience any major hindrances because I planned my course of action. And because I outlined my objectives and goals each week, I was able to pace myself through the data collection period. With every plan, there must be an alternative. If you start with a general topic and narrow down to a more precise and condensed focus, creating a project that is legitimate for a preferred service learning site is easier. It also presents fewer issues in settling on a topic.

Limitations: In pursuit of a goal

When conducting research, the presence of constraints and hindrances can always be an issue. In order to support the information gathered pertaining to the prevalence and incidence rate of HCC in female and male Gambians; I needed to use a representative sample. Unfortunately, I was only able to use information from the RVTH about HCC patients. This in turn would not be suggestive of a representative sample, but a correlation with previous studies and literature. Whilst interviewing patients and doctors, I did not have a specific method for choosing candidates for interview about clinical treatment of HCC and therefore used both doctors and patients that had treated or had been diagnosed with HCC, respectively and who felt comfortable enough to speak with me about this topic. In order to conduct random sampling, it would have required a lot of effort contacting all alive, coherent patients and willing doctors for an interview. This presented too many difficulties. However for statistical and analytical purposes, interviewing doctors that I worked closely with would be more willing to share their personal thoughts and opinions as well as factual information about clinical treatment of HCC.

I also encountered another limitation – time restraints. During the mid-way mark of my duration in The Gambia, I realized, after thorough research of the causes and influences of HCC, that traditional medicine had a significant influence on the health of ailing individuals. Although, I was able to consult a credible source for information about traditional medicine, the director of the National Traditional Medicine Program, I did not have enough time to gather detailed information about specific healers and their treatments for HCC. The information was passed through the director and therefore may have minimized the descriptions and details of plant names, exact protocol treatments and specific diagnosis tools.

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