INVESTIGATING THE RELATIONSHIP BETWEEN SOME SELECTED DISEASES HEPATITIS (A,B AND C) AND LIVER CIRRHOSIS

(CASE STUDY OF Unilorin University UITH, Kwara)

BY

IBRAHIM ABDULHAKEEM

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CERTIFICATION

This is to certify that this project was carried out by Ibrahim Abdulhakeem with matric number HND/23/STA/FT/0027.This project has been read and approved as meeting the standard requirement for the award of Higher National Diploma in the Department of Statistics, Institute of Applied Science, Kwara State Polytechnic, Ilorin.

_____	_____
MRS.YUSUF.G.A	**DATE**
(Project Supervisor)	
_____	_____
Miss. AJIBOYE R.A	**DATE**
(Project Co-ordintator)	
_____	_____
MRS. ELEPO T.A	**DATE**
(Head of Department)	
_____	_____
(External Examiner)	**DATE**

DEDICATION

This project is dedicated to Almight Allah for his infinity mercy on me and for making me to see the end of this program, Higher National Diploma (HND) and for his Divine wisdom, Knowledge and understanding throughout the academic sessions.

In addition to my lovely and caring parents MR. AND MRS IBRAHIM for their financial and moral support throughout this program and also to siblings and relatives may Almighty Allah reward you all.

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ABSTRACT

This project titled "investigating the relationships between Hepatitis (A, B, C) and Liver Cirrhosis" aim at investigating the relationship among some selected cases of diseases. Secondary data was used, the data was collected for eleven consecutive years (2013-2023) from the record department of University of ilorin Teaching Hospital (UITH), Ilorin Kwara State Analysis was carried out suing Spearman Correlation and Friedman Test. The result obtained from the spearman correlation showed that Hepatitis A has a low relationship with other selected diseases. It was equally revealed from the Friedman test that the variations in the selected cases of disease are not the same and using post hoc test, It was discovered that Hepatitis A is the major significant difference. It was recommended that Awareness and enlightens on improved personal hygiene, targeted vaccination campaign and intensive community health education should be given to the public that could of help to prevent and control liver cirrhosis and hepatitis diseases.

Key words: Hepatitis (A, B, C), Liver Cirrhosis, Spearman Correlation,

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CHAPTER ONE

Introduction

1.1 Background of the Study

Viral hepatitis results from inflammation of the liver, caused by a viral infection. Although “epidemic jaundice “has existed since ancient civilization, it is only in the last few decades that viral aetiologies of hepatitis have been identified. Almost all such infections are caused by five viruses, namely hepatitis D virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV), and hepatitis E virus (HEV). Viral hepatitis is a major public health concern, infecting millions of people annually; some infections subsequently lead to hepato cellular carcinoma (HCC), liver cirrhosis and fatalities among significant proportion of patients. The World Health Organization (WHO) estimated that I in 3people in the world have been infected by either HBV or HCV and 1.3 million people have died as a result of this disease in 2015. It has been reported that 2 billion people have infected with HBV approximately 185 million of those people are infected with HCV and 20 million people are infected with HEV. In high endemic regions more than 90% children get infected by HAV by the age of 10 although few develop complications. About 2.3 billion people of the world are infected with one or more of the hepatitis viruses. Hepatitis is an inflammation of the liver. The condition ban be self-limiting or can progress to fibrosis (scarring), cirrhosis or liver cancer. Liver

cirrhosis is a complication of many liver disease characterized by abnormal structure and function of the liver. The disease that leads to cirrhosis does so because they injured and killed liver cells, after which the inflammation and repair that is associated with the dying liver cells causes scar tissue to form. The literature documenting that hepatitis A, hepatitis B. and hepatitis C superimposed on chronic liver disease (CLD) is associated with high rates of morbidity and mortality has been reviewed. There is sample evidence that hepatitis A,B and C vaccination is safe and immunogenic in patients with mild to moderate CLD, although vaccination is less effective in those with decompensate cirrhosis or after liver transplantation. These observations have led to vaccine recommendations in patients with CLD that include hepatitis A and B vaccine in addition to pneumococcal and influenza vaccines. In spite of these official recommendations, most patients are not protected against one or more of these vaccine CLD and results of hepatitis vaccination of this population are reviewed.

HEPATITIS A IN PATIENTS WITH CHRONIC LIVER DISEASE (CIRRHOSIS)

Hepatitis A is one of the most common infectious diseases worldwide, with approximately 1.4 million clinical cases of hepatitis. Lateef AO, Aprielona LK (2000). In the United State, hepatitis A accounts for approximately half of all reported cases or viral hepatitis, with approximately 61,000 cases reported in 2003, (WHO/USAID informal consultation). Hepatitis A has been shown to have a

substantial economic burden in industrialized countries, e.g., annual costs in the United States exceeded $480 million in 1997. Recent studies show that the incidence of hepatitis A virus (HAV) infection has declined, especially in younger individuals which is attributed to implementation of hepatitis A immunization policies as well as advances in environment hygiene. Thus, there is the emergence of a new cohort of younger persons without antibody to HAV (anti-HAV) who are at risk for HAV infection. Older adults, foreign-born individuals, African Americans as well as persons with CLD are more likely to have had prior hepatitis A is usually asymptomatic in younger children, but the majority of older children and adults have a symptomatic illness with jaundice. HAV infection is usually a self-limited illness with recovery within 2 month but approximately 100 persons die of fulminate hepatitis each year in the United State. The case-fatality rate of hepatitis A is highest in adults older than 50 years of age (1.8%, versus 0.3% across all ages) and as will be reviewed, patients with CLD. Thus as hepatitis A becomes less common, the burden of new infection is shifting from children to adults, who have a higher frequency of clinically severe hepatitis, including fulminant disease. Moody A. (2002). Data available from a large outbreak of acute hepatitis A in Shanghai in 1988 and from cases of hepatitis A reported to the Centers for Disease Control and Prevention (CDC) between 1983 and 1988 demonstrated that HAV infection was more severe in patients with preexisting CLD. Acute hepatitis A superimposed on

chronic hepatitis B virus (HBV) infection was associated with a 5.6-fold and 29-fold increased risk of death, respectively, in the Shanghai outbreak and the CDC analysis of reported cases. In addition, there was a 23-fold increased risk of death in the CDC study in patients with acute hepatitis A superimposed on miscellaneous types of CLD. A matched case-control study using mortality files from the National Center for Health Statistics confirmed the association between fatal hepatitis A and underlying CLD. In this study, investigators compared the prevalence of CLD in subjects whose immediate cause of death was listed by ICD-9 codes as hepatitis A (n =1429) versus two controls groups whose immediate cause of death was listed as gastrointestinal hemorrhage (n = 2376) or biliary-pancreatic disease (n =2477). The percent of subjects dying secondary to hepatitis A and having a secondary diagnosis of CLD was 63% versus 8% and 11% with a diagnosis of CLD in the two control groups of gastrointestinal hemorrhage and biliary-pancreatic disease. A prospective 7-year study from Italy demonstrated a remarkably high incidence of acute liver failure (41%) and death (35%) in patients with acute hepatitis A and preexisting chronic hepatitis C virus (HCV) infection. In contrast to the shanghai and CDC studies cited above, this prospective study did not show higher mortality of acute hepatitis A in patients with chronic hepatitis B, although I of 10 patients had a complicat;ed course with a peak serum bilirubin of 28 mg/dL. This study requires confirmation. because two large reviews of fulminant hepatitis A in tertiary care

centers did not reveal a large number of cases with underlying chronic hepatitis C. However. in support of the studies described above, Almasio and Amoroso reviewed die clinical course of acute hepatitis A in patients with CLI) reported in 18 papers in the literature and noted that the mortality rate ranged from 0 to 100% but was generally high.

Geneva: World Health organization 2000;pp.1-57.

HEPATITIS B INPATIENTS WITH CHRONIC LIVER DISEASE

It is estimated that worldwide at least 350’ million people are chronically infected with HBV. Although the prevalence of HBV infection in the United States is lower than in many other countries, an estimated 1.25 million individuals are chronically infected with HBV, which is likely an underestimate. The published literature regarding the outcome of HBV infection in patients with CLD has primarily addressed the impact of chronic hepatitis B superimposed on chronic HCV or hepatitis D virus (HDV) rather than the outcome of acute hepatitis B in patients with CLD. The studies of acute hepatitis B in patients with CLD are limited to a few case series, but one well-conducted study showed that patients with acute hepatitis B and underlying chronic hepatitis C had a more severe course including fulminant hepatitis on the other hand, HBV and HBV co infection appears to be clearly associated with higher rate morbidity and mortality than either infection alone. Studies of patients with HBV and HCV coinfection have uniformly shown more

severe laboratory abnormalities, higher rates of cirrhosis. Greater likelihood of the development of complications of cirrhosis, and a higher incidence of hepatocellular carcinoma (liver cancer).

HEPATITIS C IN PATIENTS WITH CHRONIC LIVER DISEASES

Chronic hepatitis C progresses to chirrosis within 20 years in an estimated 20-30% of paitents, while running a relatively uneventful course in most others. Certain HCV protein can induce derangement of lipid metabolism or alter signal transduction of infected hepatocytes which leads to the production of reactive oxygen radicals and profibrogenic mediators, in particular TGF-betal. TGF-betal is the strongest known inducer of fibrogenesis in the effect or cells of hepatic fibirosis, i.e. activated hepatic stellate cells and myofibroblasts. However, fibrogenesis procceds only when additional profibrogenic stimuli are present, e.g. alcohol exposure, metabolic disorders such as non-alcoholic steatohepatitis, or coinfections with HIV or Schistosoina mansoni that skew the immune response towards a cell reaction. Furthermore, profibrogenic polymorphisms in genes that are relevant during fibrogenesis have been disclosed. This knowledge will make it possible to identify those patients who are most likely to progress and who need antiviral or antifibrotic therapies most urgently. However, even the best available treatment. The combination of pegylated interferon and ribavirin, which is costly and fraught with side effects, eradicates HCV in only 50% of patients. While the suggestive

antifibrotic effect of interferons (IF-gamma>alpha, beta), irrespective of viral elimination, has to be proven in randomized prospective studies, additional, well tolerated and cost-effective anti-fibrotic therapies have to be developed. The combination of cytokine strategies, e.g. inhibition of the key profibrogenic mediator TGF-beta, which other potential antifibrotic agents appears promising. Such adjunctive agents could be silymarin, sho-saiko-to, halofuginone phosphodiesterase inhibitors, and endothelin –A-receptor or angiotensin antagonists. Furthermore, drug targeting to the fibrogenic effect or cells appears feasible together with the envolving validation of serological markers of hepatic fibrogenesis and fibrolysis an effective and individualized treatment of liver syrouses is anticipated. Koeleman JG (2002).

1.2 Historical Background of University of Unilorin Teaching Hospital UITH Ilorin

The University of Ilorin (UNIILORIN) was established in 1975 as a university collage affiliated with the University of Ibadan. It gained full autonomy in 1997. The University of Ilorin Teaching Hospital (UITH) is a second-generation teaching hospital established by law on May 2, 1980, and commenced operations in July 1980 using the then-General Hospital and Maternity Hospital Ilorin as temporary sites. The University of Ilorin Teaching Hospital (UITH) is a tertiary healthcare institution located in Ilorin, Kwara State, Nigeria. It serves as a teaching hospital for the University of Ilorin's medical school and provides comprehensive healthcare services to patients in Ilorin and its surrounding regions. UITH plays a crucial role

in medical education, providing training for medical students, resident doctors, nurses, and other healthcare professionals. It offers undergraduate and postgraduate medical programs, including residency training across various specialties. The hospital offers a wide range of clinical services covering various medical specialties and subspecialties. These include internal medicine, surgery, obstetrics and gynecology, pediatrics, psychiatry, ophthalmology, radiology, dermatology, orthopedics, and more. UITH is involved in medical research aimed at advancing healthcare knowledge and improving patient care. Through research initiatives, the hospital contributes to the development of new treatments, diagnostic techniques, and healthcare practices .UITH engages in community health programs and outreach initiatives to promote health education, disease prevention, and wellness in the local community. These programs may include health screenings, vaccination campaigns, and public health awareness campaigns. The hospital is equipped with modern medical facilities and infrastructure to support its clinical, educational, and research activities. This includes state-of-the-art medical equipment, diagnostic laboratories, operating theaters, intensive care units, and outpatient clinics. Overall, UITH plays a vital role in the healthcare landscape of Kwara State and Nigeria as a whole, serving as a center for medical education, research, and healthcare delivery.

1.3 Statement to the Problem

These diseases can spread among the population and can kill quite a large number of people within a short period. It can even wipe out a population. It is essential to clearly accurately map out strategies towards their reduction. This study will make an appropriapate contribution of its finding is implemented.

1.4 Aim and Objectives of The Study

The main aim of this research is to investigate the relationship among some selected cases of diseases (Hepatitis) A. Hepatitis B. Hepatitis C and Liver Cirrhosis). This would be achieved through the following objective:

i. To determine the extent of relationship among the selected diseases and

ii. To determine if variation exists among the selected cause of diseases.

1.5 Significance of The Study

A study of this kind is very important to Medical Centres and the society at large. It seeks to raise awareness and enlighten the population on the nature of the selected diseases. This study will be useful for both public and private sectors by providing an insight to the problem and remedy of the diseases. It will serve as means to guide populace who lack adequate counsel and ignorance of these diseases. This study therefore serves as an eye opener to the government, non-government Organization and society at large.

1.6 Scope of The Study

The study is limited only to cases of Hepatitis A, B, C and Liver Cirrohsis at Unilorin University teaching Hospital UITH, Ilorin, Kwara State for eleven consecutive years (2009-2019).

1.7 Limitation of Study

Carrying out a study of this nature is bound to be limited. The study is limited to only some selected causes of diseases in UITH, Ilorin.

CHAPTER TWO

Literature Review

Mackowiak Baltimore (2003), that was terrific, Emmet. A cautionary comment and then a question. I was the Epidemic Intelligence Officer in Louisiana in the early ‘70’s at the time of a terrific flood which required opening both of the New Orleans spillway and resulted in oyster growing areas on both sides of the Mississippi being contaminated with Mississippi river water. We learned a number of things as a result of the massive outbreak of oyster-associated hepatitis A that followed. One was that the oyster growing area in Louisiana are located in pristine waters and not likely contaminated unless you have a major disaster such as the one just recently occurring in New Orleans. Secondly, the procedures used to tell whether or not oyster growing beds are safe monitor the water and the oyster for fecal coliforms. Thirdly, oysters handle viruses very differently from bacteria; viruses such as hepatitis A may remain in green glands, which by the way, are oysters’ version of a liver, indefinitely. And so I would be concerned that we are on the verge of another major oyster-associated hepatitis A outbreak related to contamination of Louisiana oyster-growing to areas with Mississippi River sewage. My question is, has there been any evidence of such yet? And secondly. I have followed the techniques used to monitor oyster-growing areas sort of loosely since

the 70s and wonder if there have been any developments beyond the use of fecal coliforms to certify oyster beds safe harvesting.

Keeffe Palo Alto: (2009). One interesting bit of information is that there is a declining incidence rate of hepatitis A in the U.S. This has been reported from a number of sources and is probably the result of two things. One factor is improved environmental hygiene, and the other factor is the impact of vaccination programs around the region, because the CDC recommends hepatitis A. vaccine in all counties or states where there is a high incidence rate of hepatitis A. So we have a growing cohort of people entering early adult and middle-adult life that are now not immune to hepatitis A and are at risk. As outbreaks occur from potentially contaminated oyster, and there have been outbreaks related to other food items as well, we have increasing proportion of risk for hepatitis A. I just learned as I was coming to this meeting the day before that the CDC is going to recommend routine hepatitis A vaccination in childhood. This will get around that problem of a growing adult population at risk for hepatitis A.

Lennon Galveston Emmet: (2001). That was a very nice talk. I have two questions that are related. One is whether you could speculate on the meehanisms that are in play that result in greater pathogenicity or worse clinical outcome when hepatitis A occurs in the background of chronic hepatitis or other chronic liver diseases is it reduced hepatic reserve or altered hepatic architecture that leads to a greater disease

response, or is there an impaired immune response based on the chronic liver disease that facilitates increased replication of the invading virus? The second question, which is related to the first, is; why in hepatitis A, we find age to be strongly correlated with severity of disease. most severe forms of disease occur over the age of 55. So does the association of severe disease with pre-existing chronic liver disease extend across all ages as well?

Keffe Stan, (2008). There appears to be no definitive data in terms of the potential role of impaired reserve. In the one prospective study by Vento from the New England Journal of Medicine, all of the patients had a biopsy and many of them had mild chronic hepatitis histological even though they went high morbidity and mortality after superimposed infection with hepatitis A virus. So there is more than hepatic reserve accounting for the adverse outcomes. Secondly, your point about increasing age is particularly relevant because most patients with chronic liver disease are middle-aged or older. Thus, age probably enters into the risk of an adverse outcome from superimposed acute hepatitis A or B. for example, in the CDC data that I analyzed, there was a much higher case fatality rate than in the shanghai outbreak, because the shanghai patients were younger. So your point about the impact of age is very well taken.

Gollan Omaha Emmet, (2003), a related question on immunogenicity, with regard to hepatits B vaccine, there are a small group of patients who are non-responsive to

hepatitis B vaccination in the normal population; they are kind of comparable. Do we have any kind of logical explanation as to this kind of lowered immunogenicity and its clinical relevance? Is it all to do with the relative state of immune suppression?

Keffe John, (2008). An appropriate comparison is the dialysis population, who are relatively immune suppressed and known to respond poorly to standard doses of hepatitis B vaccine. So do patients with advanced chronic liver disease especially when decompensated, have poor function as well? it appears they simply cannot mount an adequate antibody response to the antigenic challenge from hepatitis A and B vaccine. These observations support an important role of immune function. The most dramatic situation is post-transplant when patients are formally immune suppressed with drugs, and the results of vaccination are particularly poor.

Boyer (2004) New Haven Emmet, what do we know about the duration of protection in patients liver disease as opposed to the normal population?

Keffe Jim (2001), there are no specific data regarding the duration of protection after vaccination of patients chronic liver disease. However, geometric mean titers are fairly robust after vaccinating patients, and extrapolating from what is known regarding long term immunogenicity in the general population, protection is probably long-term in patients with chronic liver disease. Long-term immunity can

be modelled based on antibody decline early after vaccination, but this modelling has not been formally studied in patients with chronic liver disease.

Hepatitis B is life threatening liver disease by highly contagious blood borne viral pathogen known as hepatitis B virus (HBV). The HBV infection is one of the principle causes of severe liver disorders, including hepatocellular carcinoma, cirrhosis and end stage liver disease. In 1963, HBV was accidentally discovered by Baruch Blumberg during his research on Australia antigen. HBV is an enveloped virus which belongs to hepadnaviridae; circular partially double stranded DNA resenting highly compact organization. The HBV is smallest known DNA virus, spherical shape with diameter of about 42nm and genomic length of approximately 3.2. The infectious virus particle, also referred as Dane particle is responsible for causing infection in approximately five percent of worlds population with 2 billion people infected with the virus and 350 million as carrier of chronic infection. The virus is responsible for 600,000 deaths each year. HBV as been recognized as an important global health problem. Tremendous efforts are being put forward by many scientist, from the world, for prevention and control of viral infection. To date, successful vaccination strategies have been developed to arrest the viral spread among various populations. The need of time is to put major emphasis on awareness about risk factors associated with transmission of hepatitis viral infection and to

equip with adequate strategies for prevention of disease at national and international level.

Hepatitis C virus (HCV) is blood borne pathogen which causes severe liver disorders including hepatocellular carcinoma hepatic steatosis, liver cirrhosis end stage liver disease and various metabolic disorders. In 1989, HCV was identified by choo et al. as a positive stranded RNA molecule related to Togaviridae or Flaviviridae. HCV has been classified into the genus hepacivirus of the family Flaviviridae. This virus is responsible for causing infection in three percent of world population with approximately `170 million people at risk of developing chronic hepatitis. Due to continuous increase in number of viral infected hepatitis patients, World Health Organization (WHO) has recognized HCV as a major global health problem. Various epidemiological patterns and worldwide surveillance strategies are being performed for prevention and control of this disease. The HCV is small spherical enveloped virion with icosahedral capsid. The structure consists of an icosahedral lipid membrane with 2 giycoprotiens (termed E1 and E2) that form heterodimers. An icosahedral nucleocapsid is thought to be present inside the viral membrane. The buoyant density of HCV in sucrose is 1.06 g/cm3, whereas in chronically individuals the density is approximately 1.17g/cm3 which might be due to viral association with antibody. HCV can live on various environmental surfaces more than 16 hours and possibly up to 4-days.

Articles were searched from google scholar and pubmed with key words of HBV and analysis of HBV DNA expression, genotypic distribution of HBV and global epidemiological patterns of HBV, HCV and analysis of HCV genome, genotypic distribution of HCV and global epidemiological patterns of HCV. The valued information was subjected for review.

The nucleocapsid of Dane particle is about 28nm in size and constitutes hepatitis B core antigen. It is involved in packaging of viral genome. The hepatitis B surface antigen (HBSAg) present on the surface of HBV particle and 22nm particles and tubular form, act as complex antigenic determinants. The infectious Dane particle acquires its membrane by budding or through secretory transport mechanisms via Golgi apparatus and endoplasmic reticulum. Membrane at outer envelope forms HBSAg which contains three viral surface proteins named according to their size of small, middle and large as HBmAg. HBmAg and HBIAg respectively. These proteins are encoded on same open reading frame (ORF) that encodes 3 start codons and get overlaps with polymerase ORF.

The pregenomic RNA is the largest transcript which serves as template for viral replication. The only enzyme encoded by viral genome, which reserves transcribes the pregenomic RNA, is viral polymerase and this enzyme is also located inside the nucleocapsid. The alternative translation products of core gene include hepatitis B core antigen and hepatitis B envelope antigen (HBeAg). For the translation of

HBeAg, an upstream pre-core region with ATG codon is required. The HBeAg undergoes post translational modification. It plays very prominent role in molecular diagnosis of HBV infection by acting as an active market for viral replication. The

HBeAg (acting as antigenic determinant) also circulates in serum as soluble protein. There are two DNA strands known as long (negative) strand and short (positive) strand. The L strand contains fixed length of 3.2 kb, but the length of S strand is variable at its 3` end. The S strand usually spans 50% to 100% of the L strand.

There exists four conserved partially overlapping ORF in L strand, but in case of S strand, no partially overlapping ORF exist. Along with many DNA replication signals, the viral genome also contains two enhancer elements, six start codons, four promoters and poly adeylation signal motif. The viral genome encodes for only seven protiens, that is pre-core/core proteins, the polymerase are capped and polyadeylated, like pre-C/C (3.5kb in length), pre-S (of 2.4 kb), smRNA (of 2.1 kb) and an occasional xmRNA (of approximately 0.7kb) all of these HBV transcripts have 3 end common which has been created by the polyadenylation signal core gene. The level of HBeAg and igG anti-HBe remains persistently detectable during chronic HBV infection. The level of HBeAg for more than six months indicates occurrence of chronic infection. A test negative for IgM anti-HBc together and positive for the HBsAg in same serum sample indicates onset of chronic infection in HBV infected patient.

Some of the possible causes of persistent viral infection includes high viral load, high replication viral inhibition of antigen presentation, viral mutations that antagonize antigen recognition, immunosuppressive effects of virus, immunologic tolerance, exhausted T cell response, insufficient co-stimulation of virus specific T-cells, inefficient viral presenting cells ands alteration of T Helper Type 1and 1 Helper Type 2 balance. On average the incubation period of HBV is approximately 60 -90 days among patients of clinical illness (jaundice) the prevalence of HBV is approximately less than 10% for the patients of less 5 years but the prevalence rate ranges from 30%-50% for patients of 5 years or above for HBV infection the acute case fatality rate is approximately in the range of 0.5%-1% Generally the rate of chronic infection among patients of less than 5 years of age, is 30%-90%. But the rate of chronic infection lies between 2%-10%for the patients of 5 years of age or more The premature mortalitv rate from chronic liver disease is approximately 15%-5%The HBN has strict tissue tropism to the liver the virus infected hapatoytes produces large amount of HBsAg particles which lack the DNA The viral DAN is capable of integrating into host chromosome. Normally' HBV is not cytopathic itself instead in case of chronic hepatitis B disease. the liver damage takes place because of immune clearance phase of host against HBV infected hepatocytes

The primary liver carcinoma is considered 5th most frequent cancer of world and heat carcinoma is the major type or primary liver carcinoma. In many areas of the

world, more than 85% of hepatocellular carcinoma retains markers against hepatitis B and hepatitis C. Two treatments options are available for the prophylaxis against HBV, which includes HBV and hepatitis B immune preexposure and post-exposure, protection against HBV infection. The hepatitis B vaccine is recommended. The vaccine is capable for long term protection against HBV infection. The hepatitis Bimmune globin can only provide temporary protection for approximately 3-6 months. This treatment option is usually recommended for post-exposure settings. Hepatitis B viral form mutants are developed in some patients. These viral mutants are resistant against one or more antiviral drugs. Researchers tend to develop novel antiviral therapeutic option in order to prevent resistance and minimize viral load.

CHAPTER THREE

Methodology and Data Presentation

3.1 Method of Data Collection

Basically, there are two main categories of data collection; these are primary and secondary

i. **Primary Data:** it is a data collected by the investigator originated for the purpose of inquiry in hand. These data can be collected through direct observation, interviewing, questionnaire and telephone. It is more reliable since it is collected for the first time by the investigator.

ii. **Secondary Data:** these are data that have been already compiled and made available by an authorized agent or body. The data is not originated by the investigator for inquiry at hand but have been used for particular purpose by someone else. It has advantage of saving time and cost when collecting.

The data used in this project is a secondary data, which was collected on yearly basis from Ahmadu Bello University Teaching Hospital, ABUTH, Zaria Kaduna State, which covers a period of 11-years from 2009-2019.

3.2 Nonparametric Tests

Nonparametric statistics is the branch of statistics that is not based solely on parameterized families of probability distributions (common examples of parameters are the mean and variance). Nonparametric statistics is based on either

being distribution-free or having a specified distribution but with the distribution's parameters unspecified. Nonparametric statistics both descriptive statistics and statistical inference.

Non parametric statics refers to a statistical method in which the data is not required to fit a normal distribution. Non parametric data does not rely on numbers, but rather ranking or order. Ranks are provided based on the magnitude of the variation of values between study groups.

3.3 Friedman Test

Friedman test is a non-parametric test, which is in form of two-way analysis of variance design. The layout/design for Friedman test consist of n-rows of subjects or individuals and k-columns of conditions or items to be compared. To compute the test statistic, we first rank the scores for each row separately and then sum the ranks for each column to obtain Rj.

We may write the pair hypothesis as follows

H0: $\mu 1 = \mu 2 = ,\ldots,= \mu K$ (The K treatment are all equally effective)

H1: $\mu 1 \neq 2 \neq ,\ldots,\neq \mu K$ (The K treatment are not all equally effective)

3.3.1 Test Statistic

The test statistic for Friedman test is given by:

$$= \frac{12}{nk(k+1)} \sum_{j=1}^{k} R_j^2 - 3n(k+1)$$

Adjustment needs to be if there are many ties present. The Friedman statistic adjusted for the presence of ties is given by:

$$\mathrm{F} = \frac{(\mathrm{K}-1)[\sum_{j=1}^{k} nC_1]}{A_1 - C_1}$$

$$= \frac{(\mathrm{K}-1)[\sum_{j=1}^{k} [R_j - \frac{n\,[k+1]}{2}]^2}{A_1 - C_1}$$

Where

$\mathrm{A_I} = \sum_{i=1}^{n} \sum_{j=1}^{k} R[\mathrm{X_{ij}}]^2$ and $\mathrm{C_I} = \frac{\mathrm{n(k+1)^2}}{4}$

R ($\mathrm{X_{ij}}$) Is the rank of the (i, j)th observation.

3.3.2 Multiple Comparisons

If the null hypothesis is rejected, the need of multiple comparison arises. Treatments i and j are considered different if the following inequality is satisfied.

$$\left|R_i - R_j\right| > t_{(n-1)(k-1)(1-\frac{a}{2})} \left[\frac{2\left(nA_I - \sum R_j^2\right)}{(n-1)(k-1)}\right] \frac{1}{2}$$

YEAR	HEPATITIS A	HEPATITIS B	HEPATITIS C	LIVER CIRRHOSIS
2013	20	32	60	62
2014	25	42	71	73
2015	10	39	52	57
2016	15	44	50	52
2017	9	47	61	55
2018	17	39	49	50
2019	7	25	38	39
2020	11	40	40	42
2021	10	28	30	32
2022	12	11	19	20
2023	11	10	21	22

$$= t_{(n-1)(k-1)(1-\frac{a}{2})} \left[\frac{2n\ (A_{I-}C_I}{(n-1)(k-1)}\left(1-\frac{F}{n(k-1)}\right)\right]^{\frac{1}{2}}$$

Where

$t_{(n-1)(k-1)(1-\frac{a}{2})}$Is the $(1-\frac{a}{2})$ quantity of the t-distribution with $(n-1)(k-1)(1-\frac{a}{2})$ degrees of freedom

If there are no ties,$A_I = \frac{nk(\ k+1)(2k+1)}{6}$ and

$$A_I\ -\ C_I = \frac{nk\ (k+1)(k-1)}{12}$$

3.4 Data Presentation

CHAPTER FOUR

Analysis and Discussion of Results

4.1 Introduction

This chapter is devoted to data analysis. The method describe in chapter three would be employed for the analysis.

The analysis would follow the following order below

i. To determine the extent of relationship among the selected diseases.

ii. To determine if variation exists among the selected cases of diseases.

To determine the level of relationship among the selected case of diseases

Table 4.1: Correlation Coefficients Table

	Hepatitis A	Hepatitis B	Hepatitis C	Liver cirrhosis
Correlation Coefficient	1.000	.153	.301	.388
	.	.653	.368	.238
	11	11	11	11
	.153	1.000	.793**	.697*
	.653	.	.004	.017
	11	11	11	11

	.310 .368 11 .388 .238	.793** .004 11 .697*	1.000 . 11 .973**	.973** .000 11 1.000

******. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Findings: The result obtained in table 4.1 above contained the spearman correlation among the selected case of disease. The result showed that Hepatitis A has a low relationship with other diseases while the other disease has a high relationship among others.

To determine if variation exist among the selected case of diseases.

Ho: The variations in the selected cases of diseases are the same

H1 : The variations in the selected cases of diseases are not the same

Level of significance: $\alpha=0.5$

Test statistic: $F= 12 \sum R^2j – 3n(k + 1)$

Decision Rule: Reject Ho if p- value < significance level

Friedman Test

Table 4.2 The Mean Ranks of the selected cases of diseases

Ranks

	Mean RANK
Hepatitis A	1.18
Hepatitis B	1.86
Hepatitis C	3.05
Liver	3.91
Cirrhosis	

Table 4.3 Computations

Test Statistic[a]

N	**11**
Chi-	**29.477**
Square	
Df	**3**
Asymp	**.000**
Sig.	

a. Friedman Test

Conclusion: Since the p-value (0.000) in table 4.5 is less than the significance level ($\alpha = 0.05$), we reject Ho and it is therefore concluded that the variations in the selected cases of diseases are not the same. Since the null hypothesis is rejected, hence we produced to multiple comparison test.

Table 4.4 Computation of multiple comparisons

Disease Pairings	t-test value	Asymp. Sig	Status
Hepatitis A & Hepatitis B	-4.582	0.000	Significant
Hepatitis A & Hepatitis C	-5.903	0.000	Significant
Hepatitis A & Liver Cirrhosis	-6.171	0.000	Significant
Hepatitis B & Hepatitis C	-1.923	0.069	Not Significant
Hepatitis B & Liver Cirrhosis	-2.120	0.047	Significant
Hepatitis C & Liver Cirrhosis	-0.166	0.870	Not Significant

Findings: The result obtained in table 4.4 above showed the result of comparison test. Based on the result obtained, it is concluded that Hepatitis A is the major difference that is significant.

CHAPTER FIVE

Summary, Conclusion and Recommendations

5.1 Summary

This project titled “Investigating the relationships between Hepatitis (A,B,C) and Liver Cirrhosis”. The data for eleven consecutive years (2013-2023) was obtained from the record department of Unilorin University Teaching Hospital (UITH), Ilorin Kwara State. The statistical tools used for the analysis were Spearman Correlation and Friedman test. Table 4.1 contained the correlation matrix among the selected diseases, it was observed that Hepatitis A is the only disease that has a low relationship with others. Table 4.3 contained the Friedman test result, the result obtained showed that the null hypothesis cannot be accepted since the p value of 0.000 is less than the significance level of 0.05. It was therefore concluded that there exist significant differences among the selected diseases and a further test of comparison was performed to known the disease that causes the significant difference. It was observed that Hepatitis A is the significant.

5.2 Conclusion

Based on analysis, it was concluded from both analysis Spearman Correlation and Friedman test that the variations in the selected cases of diseases are not the same. The result obtained using multiple comparisons shows that Hepatitis A is the

significant disease among the selected diseases and it has very low relationship compare to other diseases.

5.3 Recommendations

Based on the procceeding findings on the results of the analysis, the following are hereby recommended

- ssAction plan should be structured around direction, information, intervention, delivering, financial and innovation scheme towards all hepatitis viruses, most especially hepatitis A
- Awareness and enlightens on improved personal hygiene, targeted vaccination campaign and intensive community health education should be given have been to the public that could of help to prevent and control liver cirrhosis and hepatitis diseases.

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