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Research Article

Lipid Profile, Albumin and Zinc among Patients with Human Immunodeficiency Virus and Drug Resistant Tuberculosis Co-Infection in Ojo, Lagos State

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Abstract

Human Immunodeficiency Virus (HIV) progressively destroys the immune system and weakens human's ability to fight infections and diseases. Tuberculosis is the most common opportunistic infection in HIV infected subjects. Most patients with pulmonary tuberculosis have low body nutrients and hypocholesterolemia, and lower values were strongly associated with mortality in these patients. Unfortunately, previous studies cannot unveil whether hypocholesterolemia has any link with a patient developing DR-TB.

This descriptive cross-sectional study was carried out to determine the relationship between Drug resistant tuberculosis, (DR-TB), lipid parameters, albumin and zinc among Human Immunodeficiency Virus (HIV) infected patients. Open Source Epidemiological Statistics for Public Health and Statistical Package for Social Sciences software packages were used for statistical analysis. Data was expressed as mean + standard deviation. Analysis of variance (ANOVA) was used to compare mean differences between groups and determine association between markers of malnutrition, lipid parameters and disease severity and results were regarded as significant at $p \leq 0.05$. Post Hoc test was used to determine mean differences in the parameters across the groups.

Lipid parameters, Albumin and Zinc were lowered in subjects with HIV and Tuberculosis co-infection when compared with the controls. Furthermore, the levels of TC, TG, LDL-C and Albumin were significantly lowered in subjects with HIV and Drug Resistance-Tuberculosis co-infection when compared with those with HIV and ordinary TB co-infection. It was evident from this study that low levels of plasma lipid parameters, Albumin and Zinc where are related to Human Immunodeficiency Virus and Tuberculosis co-infection. Furthermore, lower levels were observed in cases of HIV and Drug Resistant tuberculosis co-infection.

Keywords: Lipid Profile; HIV; Co-Infection; Tuberculosis; Drug Resistant

Abbreviations

ANOVA: Analysis of Variance; DR-TB: Drug Resistant Tuberculosis; HDL-C: High Density Lipoprotein-Cholesterol; HIV: Human Immunodeficiency Virus; LDL: Low Density Lipoprotein-Cholesterol; LP: Lipid Profile; NFELTP: Nigeria Field Epidemiology and Laboratory Training Program; MDR-TB: Multi-drug Resistant Tuberculosis; RT-PCR: Reverse Transcription Polymerase Chain Reaction; TC: Total Cholesterol; TG: Triglyceride.

Introduction

Human Immunodeficiency Virus (HIV) destroys human immune system thereby producing a set of symptoms and infections called Acquired Immune Deficiency Syndrome (AIDS). The virus progressively destroys the immune system thereby making infected individuals susceptible to opportunistic infections. In a healthy host, opportunistic infections do not usually cause disease, but can cause disease in individuals with weak immune system such as those with HIV/AIDS. These infections can be caused by

many different organisms, including bacteria, viruses, parasites, or fungi [1]. Common opportunistic infections in HIV/AIDS patients include Tuberculosis, Cryptococcal meningitis, *Pneumocystis* pneumonia and Candida infection.

Tuberculosis (TB) is an infectious and contagious disease which develops under conditions of deficient immunologic response [2]. It is caused by microorganism known as *Mycobacterium tuberculosis* (MTB). *Mycobacterium tuberculosis* which is also known as tubercle bacillus is a pathogenic bacteria species of the family Mycobacteriaceae. It forms a localized infection in the lungs after inhalation. Infection with *Mycobacterium tuberculosis* does not necessarily lead to active disease as the immune response of most individuals can successfully contain it, but not eliminate the infection [3]. Tuberculosis is characterized by symptoms such as unexplained cough, dehydration, vomiting, unexplained tiredness, loss of weight, high remittent or intermittent pyrexia, loss of appetite, severe cough sometimes with blood in the sputum, exhaustion and night sweats [4].

Tuberculosis can be diagnosed through microbiologic, genetic, immunogenic and biochemical methods. The bacteria that cause tuberculosis can develop resistance to the anti-microbial drugs used to cure the disease. Drug resistant tuberculosis, (DR-TB) is tuberculosis that does not respond to at least either Isoniazid or Rifampicin, the two most powerful anti-tuberculosis drugs. Mismanagement of tuberculosis treatment and person to person transmission are reasons DR-TB continues to emerge.

Active TB is an acute inflammatory condition associated with tissue injury due to increased generation of free radicals and Reactive oxygen species (ROS). ROS and Reactive Nitrogen Intermediates (RNI) are produced as a consequence of phagocytic respiratory burst [5]. Furthermore, the disease process of TB involves cellular immunity and phagocytosis of *Mycobacterium tuberculosis* by macrophages and releases of interferons, TNF-α and other cytotoxic molecules. Phagocytic activity of macrophages, neutrophils and monocytes also generates ROS and free radicals that not only have destructive effect on serum lipids (by lipid peroxidation) but also contributes to immune suppression. The degree of inflammation determines the severity of the disease as indicated by erythrocyte sedimentation rate and acute phase protein C-reactive protein (CRP) [6].

Albumin is an important protein produced in the liver in the body. It is the most abundant protein in the blood which maintains oncotic pressure in the capillaries. Albumin ensures transfer of vital nutrients and hormones while also maintaining growth and tissue repair in the body. Zinc is one of the most abundant essential trace elements in the body. It is released from food as free ions during the food digestion. Zinc plays an important role in innate immunity. Reduced micronutrient intake involving: (Vitamins A, C and E as well as Selenium and Zinc) has been associated with impaired immunity (UNAIDS, 2010). Literature search revealed that not much study has been designed to examine the relationship between nutrition and the incidence of TB or its severity. It is however a difficult task to determine accurately what the nutritional status of an active TB patient was prior to developing active TB.

Most subjects with HIV and pulmonary tuberculosis infections have low body nutrients and low serum cholesterol levels, and lower values were strongly associated with mortality in these subjects. Although very scantily investigated, this inverse association has been mentioned by several authors [7-9]. Unfortunately, previous studies cannot unveil whether the level of hypocholesterolemia has any link with a subject developing multidrug resistant tuberculosis. Therefore, the outcome of this study is expected to generate empirical data for the levels of lipid profile in HIV and Drug Resistant Tuberculosis co-infected subjects in Ojo, Lagos State.

The overall aim of this study was to compare the Total Cholesterol (TC), Triglyceride (TG), High Density Lipoprotein Cholesterol (HDL-C), Low Density Lipoprotein Cholesterol (LDL-C), Albumin and Zinc in HIV and Drug Resistant-Tuberculosis co-infected subjects and HIV and ordinary Tuberculosis co-infected subjects.

Materials and Method

Study area

The study was carried out in the Medical Laboratory wing of the Nigerian Navy Reference Hospital (NNRH), Navy town, Ojo, Lagos State. The NNRH Ojo is the main referral hospital of the Nigerian Navy (NN) and provides quality health care to naval personnel and their families at primary and secondary levels. Additionally, healthcare services are extended to members and families of sister services (Nigerian Army and Nigerian Airforce), the Police and other paramilitary organizations. Civilians within its neighborhood also benefit from her services as part of NN co-operate social responsibilities to the civil populace. Lagos is an extensive urban area in the Nigerian State. It is often regarded as the fastest growing city in Nigeria and also one of the most populous urban cities in the world. Ojo area like other parts of Lagos metropolis is made up of a complex mix of people from various parts of Nigeria.

Study design

This descriptive cross-sectional study compares the level of lipid profile and two nutrition markers (Albumin and Zinc) in HIV subjects co-infected with Drug Resistant-Tuberculosis, ordinary Tuberculosis and controls among Nigerian adults between April and December 2016.

Subjects selection

Subjects used for this study were HIV infected adults (age-range: 18-65 years), sixty nine (69) males and forty seven (47) females that were screened for Tuberculosis at the NNRH Medical Laboratory using the GeneXpert assay. Individuals that tested free of tuberculosis without any previous or present symptoms of tuberculosis or any other pulmonary diseases were taken as Controls. Subjects were further grouped into six categories based on the outcome of the GeneXpert assay. The six groups were; subjects with HIV and Drug Resistant-tuberculosis co-infection, subjects without HIV but with Drug Resistant-tuberculosis, subjects with HIV and ordinary tuberculosis co-infection, subjects without HIV infection but ordinary tuberculosis, subjects with HIV infection without tuberculosis and subjects with neither HIV nor tuberculosis infection. Details about socio-demographic characteristics and data on type and duration of symptoms, presence of any other disease, smoking habits, and dietary habits were recorded on a closed ended questionnaire prepared for this purpose.

Inclusion criteria

Subjects with HIV and Tuberculosis co-infection who gave their informed consent were included in this study.

Exclusion criteria

Subjects who have been on anti-retroviral drugs for not more than one year were excluded from this study. Subjects with known liver and renal disease, as well as those on anti-hypertensive drugs such as Angiotensin Converting Enzymes inhibitors and diuretics (Thiazide) that alter plasma lipids and zinc were excluded from this study. Individuals who are chronic alcoholics and abusers of cigarette were also excluded from this study.

Specimen collection and storage

After an overnight fast (9-12 hrs), 5ml of peripheral venous blood was drawn from the cubital vein of each subject using aseptic technique in plain gel vaccutainer container. Specimens were then centrifuged at 3000rpm to separate the serum within one hour of blood collection and stored at -200C until analyzed for Total Cholesterol, Triglyceride, High Density Lipoprotein-Cholesterol, Low Density Lipoprotein-Cholesterol, Albumin and Zinc.

Results

One hundred and sixteen (116) subjects were enrolled for this study consisting of twelve (12) HIV and drug resistant-tuberculosis co-infected subjects (six females and six males), eighteen (18) drug resistant-tuberculosis subjects without HIV infection (six females and 12 males), ten (10) subjects with HIV and ordinary tuberculosis co-infection (three females and seven males) and thirty three (33) subjects with ordinary tuberculosis infection only (13 females and 20 males). Others were twenty five (25) HIV-infected subjects without tuberculosis (10 females and 15 females) and eighteen (18) subjects with neither HIV nor tuberculosis infection (nine females and nine males).

The mean ages of the subjects were 42.3 ± 11.0 years, 38.2 ± 12.8 years, 36.6 ± 9.5 years and 36.4 ± 13.4 years for subjects with HIV and Drug Resistant-tuberculosis co-infection, subjects without HIV but with Drug Resistant-tuberculosis, subjects with HIV and ordinary tuberculosis co-infection and subjects without HIV infection but ordinary tuberculosis respectively. The mean ages of subjects with HIV infection without tuberculosis was 41.3 ± 11.7 years while that of subjects with neither HIV nor tuberculosis infection was 43.9 ± 16.7 years.

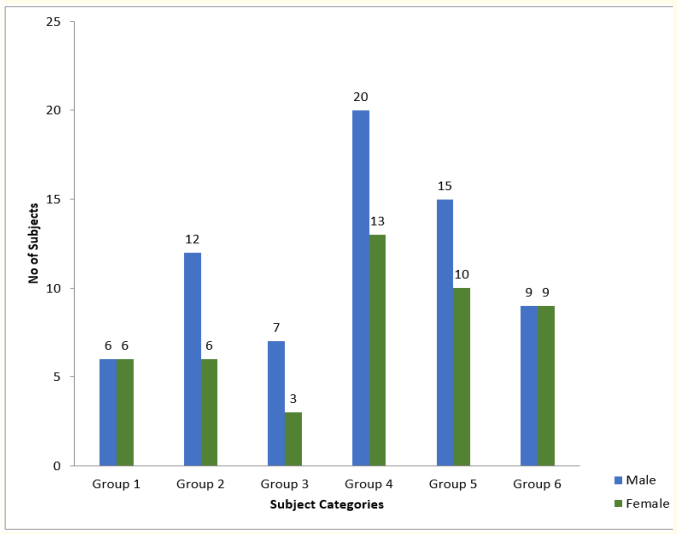

Figure 1: Gender Distribution of Subjects by Groups.

The figure above shows that majority of the subjects in this study were males.

The levels of TC, TG, HDL-C, LDL-C, Albumin and Zinc were lowered in subjects with HIV and Tuberculosis co-infection when

compared with the controls. Furthermore, the levels of TC, TG, LDL-C and Albumin were significantly lowered in subjects with HIV and Drug Resistance-Tuberculosis co-infection when compared with those with HIV and ordinary TB co-infection.

Table 1 above shows the result of analysis of variance (ANOVA) between groups across each of the parameters. There was an overall statistically significant difference in the means of all the lipid parameters analyzed including Albumin and Zinc.

Parameters						
Subjects	**TC (mmol/l)**	**TG (mmol/l)**	**HDL-C (mmol/l)**	**LDL-C (mmol/l)**	**Albumin (g/l)**	**Zinc (µmol/l)**
Group 1 (n = 12)	3.4 ± 0.41^{a}	1.6 ± 0.22^{a}	1.4 ± 0.32^{a}	1.2 ± 0.29^{a}	32.0 ± 3.91^{a}	66.1 ± 5.59^{a}
Group 2 (n = 18)	3.3 ± 0.62^{a}	1.6 ± 0.24^{a}	1.4 ± 0.21^{ab}	1.1 ± 0.38^{a}	36.1 ± 5.42^{b}	71.1 ± 3.42^{b}
Group 3 (n =10)	3.8 ± 0.63^{a}	1.7 ± 0.52^{a}	1.1 ± 0.51^{ab}	1.9 ± 0.89^{b}	38.3 ± 5.98^{bc}	72.7 ± 5.97^{b}
Group 4 (n = 33)	3.8 ± 0.71^{a}	1.7 ± 0.44^{a}	1.3 ± 0.42^{ab}	1.7 ± 0.69^{b}	39.6 ± 4.83^{bc}	74.0 ± 4.96^{b}
Group 5 (n = 25)	4.6 ± 0.82^{b}	2.1 ± 0.41^{b}	1.5 ± 0.41^{bc}	2.2 ± 0.41^{bc}	40.1 ± 5.82^{cd}	83.5 ± 7.95^{c}
Group 6 (n = 18)	5.0 ± 0.89^{b}	2.3 ± 0.53^{b}	1.7 ± 0.44^{c}	2.3 ± 0.52^{c}	43.4 ± 4.78^{d}	91.1 ± 7.81^{d}
F-value	18.176	9.134	4.320	8.981	8.607	38.287
p-value	0.000^{*}	0.000^{*}	0.001^{*}	0.000^{*}	0.000^{*}	0.000^{*}

Table 1: Serum Lipid Profiles, Albumin and Zinc in Subjects with HIV and Drug Resistant Tuberculosis Co-infection and HIV with Ordinary Tuberculosis Compared with Controls**.**

Key

Group 1 = HIV and drug resistant-tuberculosis co-infected subjects

Group 2 = Drug resistant-tuberculosis subjects without HIV infection

Group 3 = Subjects with HIV and ordinary tuberculosis co-infection

Group 4 = Ordinary tuberculosis infection only

Group 5 = HIV-infected subjects without tuberculosis

Group 6 = subjects with neither HIV nor tuberculosis infection

TC = Total Cholesterol, TG = Triglyceride, HDL-C = High Density Lipoprotein Cholesterol

LDL-C = Low Density Lipoprotein Cholesterol

* = P < 0.05 is significant

Post Hoc Test: means with different superscript are significantly different from each other.

Duncan's Post-Hoc test was however used to confirm where the differences occurred across the groups. Means with different superscripts are significantly different from each other and vice versa.

Figure 2 above shows that 40% of DR-TB subjects involved in the study were HIV positive while about 23% of subjects with TB alone were HIV positive. About 35% of subjects in the control group were also HIV positive.

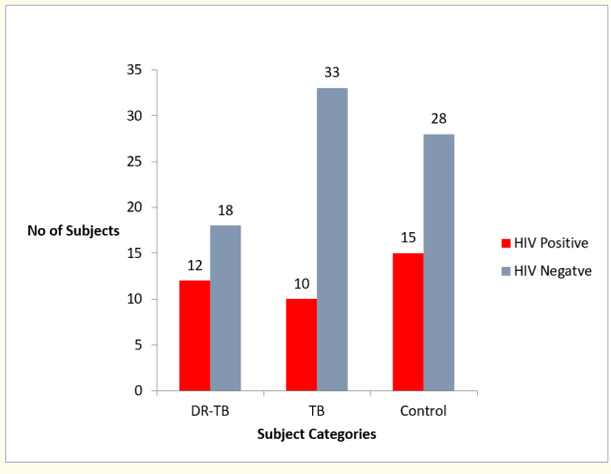

Figure 2: HIV Status of Subjects.
Key: DR-TB = Drug Resistant Tuberculosis, TB = Tuberculosis.

Discussion

Tuberculosis is the leading cause of death from a curable infectious disease [10] and as such, it is responsible for more than 1.5 million deaths every year in the world. However, it is one of the most serious opportunistic infections in HIV infected subjects as well as a leading cause of death in them. Studies in humans

and experimental animals have shown that malnutrition is an important risk factor for the development of tuberculosis [11,12], hence, it is consistent with the result obtained from this study.

The study showed that lipid profile, albumin and Zinc decreases significantly in tuberculosis subject and even more among subjects with drug resistant-tuberculosis. These results supported the observation by Kanna [13] that the level of circulating lipids decreases in severe infections. Lower levels of lipid parameters such as Total Cholesterol, Triglyceride and Low Density Lipoprotein-Cholesterol are beneficial in the human body while higher level of good cholesterol (HDL-Cholesterol) is beneficial to humans as it facilitates transporting cholesterol from peripheral tissues to the liver for degradation.

Several factors appear to contribute to low plasma zinc concentration in HIV infection. Dietary insufficiency particularly among adults, poor appetite, reduced total food intake and frequent nausea and vomiting associated with HIV infection are likely to directly increase the risk of inadequate zinc intake. Reduced Zinc level causes impaired cell-mediated immunity and compromises neutrophil functions, thereby lowering the micronutrient level in tuberculosis and drug resistant tuberculosis subjects. This is because zinc plays a crucial role in the normal development and function of cells mediating non-specific immunity hence its deficiency results in the reduction of the number of circulating T-cells in animals.

This study is in correlation with [7] which showed that tuberculosis subjects are at higher risk of zinc deficiency. The reduced zinc level which was observed in the tuberculosis and drug resistant tuberculosis subjects is also consistent with the reports of [11].

Lower level of Albumin observed in this study in drug resistant tuberculosis subjects may be related to the high prevalence (40%) of human immunodeficiency infection in this category of subjects. This is similar to the study by [14], where they reported significantly decreased serum albumin level in TB/HIV co-infected subjects than in subjects with tuberculosis alone. Gupta., et al. also reported significantly lower albumin level in HIV patients when compared with HIV negative patients [12].

Enwonwu, [15] in their study reported that micronutrients are compartmentalized to the tissues, lost from the body or blocked from cellular utilization in tuberculosis cases. However, the observed significantly low micronutrient status in tuberculosis subjects might be as a result of loss of appetite, nausea and vomiting caused by anti-TB drugs or anorexia, impaired absorption of nutrients or increased catabolism as previously proposed by [16].

Findings from this study further cement the association between malnutrition and tuberculosis. Malnutrition alters all defence mechanisms, including anatomic barriers, cell-mediated immune responses, phagocytic cell/microbial functions and humoral immunity function (antibody and complement responses) among many others. It compromises barrier function, allowing easier access by pathogens and compromises immune function thereby, decreasing the ability of the host to eliminate pathogens once they enter the body.

This study has further established that nutrition is an important susceptibility factor for any infection. However, just as malnutrition can lead to tuberculosis, tuberculosis can also lead to malnutrition [17]. From this study, it can be established that there is a direct correlation between higher degree of hypolipidemia, nutritional deficiency and immune suppression.

Micronutrient malnutrition in tuberculosis subjects may contribute to advancement of latent tuberculosis to active tuberculosis and possibly to drug-resistant tuberculosis [18]. Hence, several studies have reported that patients with active pulmonary TB are malnourished as indicated by reductions in lean mass, anthropometric indexes and micronutrient status. Malnutrition compromises barrier function, allowing easier access by pathogens and compromises immune function thereby, decreasing the ability of the host to eliminate pathogens once they enter the body. Lipids are important constituents that determine nutritional status and at the same time participate in immune function [19].

Furthermore, tuberculosis is a leading cause of death in HIV infected persons and HIV infection is the most potent risk factor for developing active tuberculosis from a latent tuberculosis infection. This study has further revealed that HIV infection is an important predisposing factor for subjects to develop tuberculosis and drug resistant tuberculosis. However, there appears a higher correlation between HIV infection and drug resistant- tuberculosis as represented in Figure 2. This however, is in correlation with the report from Rajendra., *et al*. (2012). The report revealed that of the 9.4 million incident cases of TB in 2008, an estimated 1.4 million

(15%) were HIV positive and WHO, 2007 also reported an estimate of 1.8 million people that died of TB in 2008, of which about 0.5 million were patients with MDR-TB/HIV co-infection [20].

Conclusion

It was evident from this study that low levels of lipid parameters, Albumin and Zinc were observed in Human Immunodeficiency Virus and Tuberculosis co-infection. Additionally, lower levels were observed in cases of HIV and Drug Resistant tuberculosis co-infection. Subjects with Human Immunodeficiency Virus infection have low serum lipid parameters; (Total Cholesterol, Triglyceride, HDL-C and LDL-C) as well as low levels of serum albumin and Zinc and are therefore prone to developing tuberculosis.

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