

Pattern of Changes in Some Biochemical Indicators and Prevalence of HIV Seropositive People Co-infected with Tuberculosis at FMC, Owerri, Imo State

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Abstract

The purpose of this study was to count the number of human immunodeficiency virus (HIV) patients receiving antiretroviral therapy (ART) who were also infected with tuberculosis (TB) and to evaluate the patients' changes in certain biochemical parameters at the Federal Medical Centre in Owerri, Imo State. For this study, 350 HIV-positive patients between the ages of 20 and 79 years old who gave their consent were enrolled. National serial algorithms (Determine, Unigold, and StatPak) were utilized for HIV testing, whereas the GeneXpert machine was used for TB testing. While 4 ml of blood was collected in simple vials and the serum used for biochemical analysis, the biochemical analyses were performed using autoanalyzers. The risk of having both TB and HIV was highest in people aged 70 to 79 (31.11%) and lowest in people aged 50 to 59 (10.0%). According to sex, ladies (15.7%) had a greater prevalence of co-infection than males (14.3%). Between ART and non-ART individuals in this study, the results of the biochemical examinations showed that the ART group's (test subjects') kidney indicators, urea, and creatinine, as well as their liver enzymes (AST, ALT, and ALP), were statistically higher ($P < 0.05$) than those of non-ART patients (control group). TB co-infection is more likely to affect elderly HIV-positive individuals due to their weakened immune systems by nature. Additionally, people with HIV who are not on ART run the risk of developing opportunistic infections as well as anemia. In addition to the administration of highly active antiretroviral therapy (HAART), they should be managed with additional caution. Antiretroviral medications have the potential to negatively impact vital organs like the kidneys and liver, necessitating therapeutic drug monitoring. To ensure patient compliance, more measures need to be taken by those in charge of managing these patients.

Keywords: pattern, biochemical indicators, prevalence, HIV seropositive, co-infected, tuberculosis, FMC, Owerri

Abbreviations: ART: antiretroviral therapy; TB: tuberculosis; HIV: human immunodeficiency virus; HAART: highly active antiretroviral therapy; AIDS: acquired immunodeficiency syndrome; FMOH: Federal Ministry of Health; WHO: World Health Organization; MDR-TB: multidrug-resistant TB; NAA: nucleic acid amplification; MTBC: *Mycobacterium tuberculosis* complex; RIF: rifampin resistance; SOPs: standard operating procedures; WBC: white blood cells; RBC: red blood cells; Hb: hemoglobin; PLT: platelet; PCV: packed cell volume; ESR: erythrocyte sedimentation rate; HCT: hematocrit; FSC: forward scatter; SSC: side scatter; STDs: sexually transmitted diseases; AST: aspartate transaminase; ALB: albumin; ALT: alanine transaminase; ALP: alkaline phosphatase

Introduction

The human immunodeficiency virus (HIV) is one of the most important emerging infections of the twenty-first century. It's probably one of the illnesses that affects people individually as well as families, communities, and society at large. HIV is a risk, especially in Sub-Saharan African countries [1]. HIV is a serious public health concern that is estimated to afflict 36.7 million people globally [2]. Of the 24.7 million individuals in Sub-Saharan Africa who have the disease, 11.7 million (32.0%) are now on antiretroviral therapy (ART). The percentage of people living with HIV infection in Nigeria increased from 1.8% in 1991 to 3.4% in 2015, and 44.9% of those individuals are currently on antiretroviral medication. All the states of the federation, including Abuja, have reported cases of HIV infection, and the incidence rates differ greatly from state to state and from zone to zone. The Federal Ministry of Health (FMOH) established the first HIV sentinel surveillance to track HIV/acquired immunodeficiency syndrome (AIDS) in the nation as part of its initial assessment of the HIV/AIDS situation in Nigeria. HIV is the primary cause of AIDS, a systemic illness that is marked by severe dysfunction and deteriorating humoral and cellular immune responses [3]. Hematological abnormalities have been shown to be powerful independent predictors of morbidity and mortality in HIV-infected persons, in addition to immunological consequences of HIV illness [4]. Anemia in HIV-positive patients is linked to CD4 cell depletion and the development of AIDS, making it one of the most potent predictors of HIV mortality and a poor response to ART [5]. However, lymphocyte count was used as a stand-in until CD4 count became more widely available, especially in poor countries. It has been demonstrated that ART can significantly reduce the risk of HIV transmission and avert AIDS-related disease and death [6]. There are currently 20.9 million (18.4 million–21.7 million) HIV-positive individuals who can access antiretroviral medication (ART), the most effective form of HIV care available. Thus, HIV is today a chronic infectious disease that can be treated because of the discovery of contemporary medications [7].

HIV patients who have utilized ART and those who have not have a variety of immunological, biochemical, and hematological issues. ART is frequently associated with hematological disorders such as anemia, leukocytopenia, neutropenia, thrombocytopenia, and CD4 cell depletion [3]. Biochemical indicators such as bilirubin, electrolytes, creatinine, blood urea, albumin (ALB), aspartate transaminase (AST), alanine transaminase (ALT), and alkaline phosphatase (ALP) are often altered by HIV infection, and using ART may have a deleterious effect on these conditions [6]. The advent of pharmaceutical companies, research institutions, and governments' drug expansion initiatives made highly active antiretroviral therapy (HAART), which is currently used to treat HIV infection, conceivable [8]. The introduction of HAART, which is typically a combination of two or more antiretroviral medications, has improved the quality of life for people with HIV and slowed the development of their infection to AIDS [9]. Despite its efficacy, HAART therapy has unfavorable side effects, such as diarrhea, nausea, anemia, neutropenia, an increase in bilirubin, an increase in amylase enzyme, and cytopenia [5]. Patients are at significant risk of acquiring both short-term and long-term side effects such as cardiovascular abnormalities, hepatotoxicity, and renal diseases [10]. The global effort to eliminate tuberculosis (TB) is significantly hampered by the HIV pandemic. Of the 8.7 million persons who contracted TB worldwide in 2011, 1.1 million (13%) had HIV. The major cause of death for those with HIV is TB. TB is at least partially responsible for at least one in four HIV-positive individuals' deaths. The World Health Organization (WHO) published a document on priority research questions in 2010 and an updated policy on collaborative TB/HIV activities in 2012. Both documents stress the importance of surveillance of HIV among TB patients and surveillance of active TB patients among people living with HIV in all countries to reduce the dual burden

of TB/HIV in populations at risk of or affected by both diseases. Co-infection with HIV and TB is a serious issue for global public health. Indeed, people living with HIV have a case fatality rate of 16–35%, which is about four times greater than people without HIV, making them 20 times more likely to contract TB than HIV-negative people [10].

Numerous variables, including smoking, family size, the clinical stage of HIV, the use of ART, injectable drug usage, and anemia, affect the likelihood of co-infection [11]. Additionally, it is clear that having a positive HIV test, drinking alcohol, working in agriculture, and having previously been exposed to TB are risk factors for multidrug-resistant TB (MDR-TB) [12]. Malnutrition, rapid disease progression, unusual TB presentations, delayed diagnosis, and poor treatment response all increase the effects of TB and HIV co-infection, which have a variety of health consequences that shorten the life expectancy of the infected host [13]. HIV's diversity and rate of replication increase as a result of active TB's facilitation of the transcription of HIV genes [14]. On the other hand, when the HIV clinical stage advances, the spread of the virus and extrapulmonary TB symptoms also rise [15]. Patient suffering is also brought on by frequent pyrexia, diarrhea, rapid weight loss, and wasting [16].

HIV-positive patients on ART must have regular monitoring of their hematological and biochemical markers throughout their treatment. While published data in this area is scarce, some studies have reported on hematological and biochemical changes associated with ART in HIV patients. What's more, most infected individuals also have undiagnosed TB, which affects their perception of the sickness. This study assesses the changes in hematological and biochemical markers in HIV seropositive individuals co-infected with TB in an effort to improve the prognosis of the illness after therapy.

Materials and Methods

Study area

- HIV diagnosis

Patients were identified using the national algorithm, as well as the Determine™ HIV-1/2 Stat-Pak® and Uni-Gold™ HIV test kits from Trinity Biotech Plc in Bray, Co. Wicklow, Ireland, and Alere Medical Co., Ltd. in Matsuhida, Matsudo-Shi, Chiba, 270-2214, Japan, respectively. In the event of a tie, a Stat-Pak was utilized to determine the winner.

- Tuberculosis diagnosis

All HIV-positive people had their sputum samples collected and forwarded to the microbiology lab so that the GeneXpert machine could diagnose TB.

Principle: In less than 2 h, the GeneXpert MTB/RIF assay, a nucleic acid amplification (NAA) test, can identify the DNA of the *Mycobacterium tuberculosis* complex (MTBC) and rifampin resistance (RIF) or mutation of the *rpoB* gene. The sample processing, NAA, and target sequence detection are all integrated and automated. The 81-base pair "core" region of the *rpoB* gene is amplified by the primers used in the Xpert MTB/RIF assay. The RIF-related mutations in the core region can be distinguished from the conserved wild-type sequence by the probes.

Laboratory techniques

The standard operating procedures (SOPs) of the manufacturer were strictly followed, and all reagents were purchased commercially.

- Calculation of hematopoietic parameters

Using an automated Sysmex KX-21N hematology analyzer, total white blood cells (WBC), red blood cells (RBC), hemoglobin (Hb), platelet (PLT) count, and packed cell volume (PCV) were measured in whole blood samples. The Sysmex KX-21N is a completely automated hematology analyzer designed for in vitro diagnostic use (Sysmex

Corporation, Kobe, Japan) that has the ability to assess and produce findings for hematopoietic parameters. The KX-21N uses hydrodynamic focusing with impedance for RBC and PLT counting along with fluorescence flow cytometry with a laser semiconductor to assess leucocyte differential. The sodium lauryl sulfate methemoglobin technique is used to calculate Hb levels. The Westergren method was used to calculate the erythrocyte sedimentation rate (ESR), and the Partec CyFlow Counter, an autoanalyzer that employs the flow-cytometry principle, was used to count the CD4 cells.

Sysmex theory: The KX-21N uses electronic resistance detection to measure and quantify PLT and RBC. Utilizing cumulative pulse height detection, hematocrit (HCT) is calculated as the proportion of the total volume of RBCs to the total volume of blood. Methemoglobin is created from Hb, which is then measured photometrically at 555 nm. Individual cells are suspended in a physiological solution, labeled with fluorescence dyes or absorption dyes, and then inserted under a little pressure through a flow chamber into the middle of a stream of cell-free sheath fluid. For analysis and cell sorting based on the fluorescent antibody directed against a particular surface, the light dispersed by the individual particle and the fluorescence emitted by the cells are both used. The flow cytometer's detectors catch this mixture of scattered and fluorescent light. The electronic signals generated by these detectors are then proportionate to the optical signals they have detected. Based on the size and internal structure of the cell, visible light is bent. Forward scatter (FSC) and cell volume are correlated. Side scatter (SSC) is dependent on the particle's internal complexity (*i.e.*, the shape of the nucleus, the amount and type of cytoplasmic granules, or the membrane roughness). The fluorescence-tagged particular monoclonal antibodies against the cell surface markers determine the fluorescence released by the cell. The computer stores the information that has been gathered about each cell or event. This information is then transformed and examined to reveal details about the cell populations within the sample.

▪ Biochemical parameter determination

An automated Selectra ProS chemistry analyzer was used to measure the biochemical parameters AST, ALT, ALP, creatinine, and urea levels from serum samples (Puteaux, France, and reagents supplied by ELITechGroup, Rotterdam, Netherlands). The Selectra ProS is an automated chemistry analyzer that measures analytes in samples of serum, plasma, urine, and aqueous standard solutions for in vitro diagnostic purposes in conjunction with reagents. When measuring analytes with spectrophotometric methods such as end-point, rate, and turbidimetric assays, the analyzer uses a spectrophotometric system. On the basis of the test kit results, normal ranges were reported.

Statistical analysis

In order to evaluate the data, SPSS version 22 was used. Values were presented as percentages and with a 95% confidence level for the mean and standard deviation. Tables were used to display the results.

Results

	No. Examined	No. positive	Prevalence (%)
	350	53	15.14
Total	350	53	15.14

Table 1: Overall prevalence of HIV positive patients on therapy co-infected with tuberculosis in the study population.

Age	No. Examined	No. positive	Prevalence (%)
20–29	76	9	11.84
30–39	81	11	13.58
40–49	65	7	10.77
50–59	50	5	10.0
60–69	33	7	21.21
70–79	45	14	31.11
Total	350	53	15.14

Table 2: Age-related prevalence of HIV-positive patients on therapy co-infected with tuberculosis in the study population.

Sex	No. Examined	No. positive	Prevalence (%)
Male	133	19	14.3
Female	217	34	15.7
Total	350 (100.0%)	53	15.1

Table 3: Sex-related prevalence of HIV-positive patients on therapy co-infected with tuberculosis in the study population.

Parameters	Test	Control	P-value
	(Mean \pm SD)	(Mean \pm SD)	
AST	24.00 \pm 3.50	17.50 \pm 4.70	0.000
ALT	17.50 \pm 4.70	16.90 \pm 2.40	0.000
ALP	268.15 \pm 142.63	224.48 \pm 135.53	0.039
Urea	48.40 \pm 5.20	44.7 \pm 7.2	0.001
Creatinine	1.96 \pm 0.72	1.74 \pm 0.54	0.011

Table 4: The mean (\pm SD) values of the biochemical parameters in the study population. Key: $P < 0.05$ will be taken to be statistically significant.

Discussion

According to the report, 15.14% of patients at the Federal Medical Centre in Owerri's HIV clinic unit are also infected with TB. This might be connected to the HIV pathogenesis, which depends on immunosuppression. Because of this, their immune system has been damaged to a greater extent, leaving them more vulnerable to opportunistic diseases like TB. The participants with the highest age-related prevalence of co-infection (31.11%) were between the ages of 70 and 79. The age factor is responsible for this. It is well known that immunity deteriorates with age and that opportunistic infections are more common in the elderly. The number of HIV-positive patients is typically reported to be higher in females (15.7%) than in their male counterparts, according to sex. This could be a result of young women's undeveloped vaginal tracts and readily damaged tissues making them more susceptible to the virus. Because the vaginal area is broader and more exposed to sexual secretions during sex than the mostly skin-covered penis, as well as because of hormonal changes related to childbearing that tend to weaken the body's immune system, women are also more susceptible to sexually transmitted diseases (STDs). This concurs with the 2002 United Nations Children's Fund study as well. Gender disparities in many African tribes, including the one Owerri is a member of, which prohibit young women from negotiating safer sexual practices like the use of contraception like condoms, also contribute to this rise. Instead of relying solely on socio-cultural factors affecting women's propensity to visit HIV clinics, this influence may be to blame for the rise in female prevalence. Between ART and non-ART patients in this trial, there was no statistically significant change in the PLT and RBC counts. On the other hand, non-ART patients had statistically greater WBC counts and ESR than ART patients ($P < 0.05$). The increased rate of opportunistic infection in HIV-seropositive patients not receiving ART can be explained by this increase. When compared to non-ART patients, those on ART had statistically greater Hb concentrations and PCV ($P < 0.05$). A recent research has shown that mean Hb increases dramatically in patients receiving ART, reversing HIV-associated anemia [17]. Patients on ART had significantly greater CD4 counts than non-ART patients ($P < 0.05$). Non-ART patients do have a lower count since the virus primarily targets CD4 cells and seeks to destroy them. The CD4 cells in ART patients receive assistance from antiretroviral medications, which primarily function to strengthen the immune system, increasing the count to that of healthy people in the reference range. According to the study, the ART groups' liver enzyme levels (AST, ALT, and ALP) and kidney function parameters (urea and creatinine) were considerably higher ($P < 0.05$) than those of the non-ART group. This is due to the fact that pharmaceuticals and other compounds are detoxified in the liver and kidney, and antiretroviral medications have been shown to be both hepatotoxic (harmful to the liver) and nephrotoxic (damaging to the kidneys).

Conclusion

Co-infection with HIV and TB is fairly common in FMC Owerri. Elderly HIV-positive people should be treated more cautiously in addition to taking HAART because of their innately lower immunity, which makes them more vulnerable

to TB. In addition, anemia and opportunistic infections are risks for HIV patients not receiving ART [18]. With the potential for injury to key organs such as the kidney and liver, antiretroviral drugs make therapeutic drug monitoring even more important in this era of test and treatment strategy in HIV management.

Recommendations

This research recommends routine evaluation of these hematological and biochemical parameters at every follow-up visit, testing for TB in all HIV seropositive patients, and early initiation and adherence to ART in accordance with the WHO's treatment guidelines in every eligible HIV-positive patient. Elderly HIV-positive individuals and those with low CD4 counts should get regular antibiotics, such as cotrimoxazole, to avoid the emergence of TB and other opportunistic infections. Those in charge of these patients' care need to take further steps to guarantee patient compliance. More voluntary counseling should be promoted to the public.

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