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Original article

Multidrug resistant tuberculosis in HIV positive patients and its effect on interleukin-2 and interferon- γ

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ABSTRACT

Background: This is a case control study aimed to detect plasma level of interleukin-2 (IL-2) and interferon-gamma (IFN- γ) cytokines in multidrug resistant tuberculosis (MDR-TB) co-infected with human immunodeficiency virus (HIV) patients and multidrug resistant tuberculosis (MDR-TB) monoinfected patients. **Methods:** This study determined the differences in plasma concentrations of pro-inflammatory (IL-2 and IFN- γ) cytokines in MDR-TB co-infected with HIV patients and MDR-TB monoinfected patients. Plasma levels of IL-2 and IFN- γ were measured in 130 participants (comprising 15 MDR-TB/HIV co-infected treatment naïve patients, 15 MDR-TB/HIV co-infected treatment experienced patients, 20 MDR-TB monoinfected treatment naïve patients, 20 MDR-TB monoinfected treatment experienced patients, 20 drug susceptible tuberculosis (DS-TB) co-infected with HIV treatment experienced patients and 40 apparently healthy control groups) using enzyme-linked immunosorbant assay (ELISA). **Results:** Shows that the mean plasma level of IL-2 (210.02 ± 59.27 pg/ml) measured in MDR-TB co-infected with HIV treatment-naïve patients (group 1a) was significantly ($p < 0.026$) lower compared to MDR-TB monoinfected treatment-naïve patients (244.20 ± 108.07 pg/ml). Conversely the mean plasma levels of IFN- γ was significantly ($p < 0.041$) higher in MDR-TB/HIV co-infected treatment-naïve patients (group 1a) (8.31 ± 3.56 pg/ml) compared to MDR-TB monoinfected treatment-naïve patients (group 2a) (6.89 ± 2.14 pg/ml). **Conclusion:** Our study revealed significantly reduced plasma level of IL-2 in MDR-TB and HIV co-infected patients compared with MDR-TB monoinfected subjects, suggesting a more advanced immunodeficiency in co-infected patients.

Introduction

Human immunodeficiency virus (HIV) and multidrug resistant tuberculosis (MDR-TB) have an effect on the immune system and are associated by a dysregulation of the normal balance of cytokines and the functioning of the cytokine network [1].

Studies have shown that both MDR-TB and HIV infection can suppress type-1 cytokine responses [2]. Multidrug resistant tuberculosis and HIV co-infection affects the function of the immune system and is characterized by cytokine irregularities [1,3].

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Multidrug resistant tuberculosis is a type of TB that is resistant to the two most effective first line drugs; Rifampicin and Isoniazid [4]. Multidrug resistant tuberculosis results from primary infection or may develop in the course of a patient's treatment [5]. The host-protective immune response against intracellular pathogens is mediated by the cellular immunity [6]. Cytokines are a group of low molecular weight proteins that mediate communication between cells of the immune system [7]. They contribute to chemical signaling pathways in inflammation, immune responses, and hematopoiesis [7]. The pro-inflammatory cytokines are secreted from T helper 1 cell (Th1 cells), cluster of differentiation type 4 (CD4) cells, macrophages, and dendritic cells. They are characterized by production of several interleukins (IL), IL-1, IL-2, IL-12, IL-17, IL-18, IFN- γ , and tumor necrosis factor-alpha (TNF- α) [8]. Pro-inflammatory cytokines generally regulate growth, cell activation, differentiation, and homing of the immune cells to the sites of infection with the aim to control and eradicate the intracellular pathogens, including viruses [8]. The production of IL-2 is mainly by helper T cells, it induces proliferation of activated helper T cells and cytotoxic T (Tc) cells and it also promote the growth of B cell [9]. Interleukin-2 (IL-2) can also be produced by cytotoxic T cell to lesser extent, IL-2 acts on T cells in an autocrine fashion [10]. Interleukin-2 can activate natural killer (NK) cells and monocytes. Activation of T cells results in expression of Interleukin-2 receptor (IL-2R) and the production of IL-2. The IL-2 binds to the IL-R and promotes cell division. When the T cells are no longer being stimulated by antigen, the IL-2R will eventually decay and the proliferative phase ends [11]. IFN- γ is produced by Th-1, cytotoxic T (Tc) cell, and NK cells, it inhibits viral replication, increases expression of class I and II major histocompatibility complex (MHC) stimulates phagocytosis and killing by macrophages and NK cell [12].

Material and Methods

Study area

The study was conducted in Aminu Kano Teaching Hospital (AKTH) and Infectious Disease Hospital Kano, Nigeria.

Study subjects

Group 1: a total of 30 MDR-TB/HIV co-infected patients were divided into group 1a (treatment naive)

and group 1b (treatment experienced) 15 patients each.

Group 2: a total of 40 MDR-TB mono-infected patients were divided into group 2a (treatment naive) and group 2b (treatment experienced) 20 patients each.

Group 3: a total of 20 drug susceptible tuberculosis (DS-TB) co-infected with HIV treatment-experienced patients.

Group c: apparently healthy control

Study design

This is a case control study that was conducted among MDR-TB co-infected with HIV patients.

Ethical approval

The study design and protocol were approved by the Ethics and Research Committee of Aminu Kano Teaching Hospital (AKTH) Kano. The research was carried out in accordance with the 1964 declaration of Helsinki concerning the ethical principles for medical research involving human subjects. Written informed consent was obtained from all study participants before enrolment.

Informed consent

Written informed consent was obtained from all study participants before enrolment.

Sputum samples collection and processing

The participants were counseled about sputum production at the directly observed treatment, short-course center and given wide mouthed sputum containers to produce sputum for Xpert MTB/RIF assay. The lid of sputum collection container was unscrewed, 2 volumes of Gene Xpert sample reagent was added into the 1 volume of sputum sample container (2:1 v/v), vigorously mixed and incubated for 15 minutes at room temperature. The samples were liquefied completely and no clumps of sputum are visible [13, 14].

Blood samples collection and processing

From each selected subject, a total of 5.0 milliliters of venous blood specimen was collected using a sterile vacutainer blood specimen bottles, holder and needle. Three milliliters of blood specimen was collected into a sterile ethylene diaminetetra acetic acid (EDTA) vacutainer blood specimen bottle, and centrifuged at 2000-3000 revolution per minute (r.p.m.) for 20 minutes to obtain clear unhaemolyzed plasma. The plasma were harvested into sterile plasma separation tubes and rapidly stored at -20^oC until assayed in batches; for plasma levels of IL-2 and IFN- γ . Two milliliter of the blood specimen was

collected into a sterile EDTA vacutainer blood specimen bottle, and used to re-determined and confirmed HIV-status.

Laboratory analysis

Detection of *MTB* and rifampicin resistance (MDR-TB)

Detection of *Mycobacterium tuberculosis* (*MTB*) and rifampicin resistance was carried out using Gene Xpert MTB/RIF technique (Cepheid 904 Caribbean Drive Sunnyvale, CA 94089-1189 USA) according to the manufacturer's instructions and standard operating procedure [13, 14]. The Gene Xpert system is a fully automated nested real-time polymerase chain reaction (PCR) system, which detects *MTB* complex DNA in smear positive and negative sputum samples. It simultaneously identifies mutations in the *rpoB* (gene encoding β -subunit of RNA polymerase and associated with resistance to rifampicin) gene, which is associated with rifampicin resistance. The Gene Xpert system consist of the instrument, a computer, a barcode scanner and requires single-use disposable Xpert MTB/RIF cartridges that contain assay reagent. The specimen is transferred into the Xpert MTB/RIF cartridge and entered into the Gene Xpert instrument. By starting the test on the system software, the Gene Xpert automates nucleic acid amplification, detection of the target sequence and result interpretation. The primers in the Xpert MTB/RIF assay amplify a portion of the *rpoB* gene containing the 81 base pair 'core' region. The probes are able to differentiate between the conserved wild-type sequence and mutations in the core region that are associated with resistance to RIF. Two volumes of sample reagent were added to 1 volume of sample (ratio of 2:1) and the lid is closed again. The sputum collection container is shaken vigorously 20 times. It is incubated for 5 minutes at room temperature. The specimen is shaken again vigorously 20 times, incubated for another 10 minutes. The samples liquefied completely and no clumps of sputum are visible. Using a sterile transfer pipette, the liquefied sample is aspirated into the transfer pipette. The cartridge lid is opened. The sample is transferred into the open port of the Xpert MTB/RIF cartridge. The cartridge lid is closed firmly. In the Gene Xpert system window, create test clicked. The scan cartridge barcode dialog box appeared. The barcode on the Xpert MTB/RIF cartridge was scanned using the barcode reader. The create test window appeared. The patient's information is taken. Start Test clicked. The instrument module door opened

with the blinking green light and the cartridge loaded. The door is carefully closed. The test started and the green light stopped blinking. The system released the door lock at the end of the run. The results displayed in the "view results" window of the Gene Xpert machine and recorded in the TB laboratory register.

HIV screening test

The HIV screening test was carried out using the world health organization (WHO) screening criteria for developing countries which entail the use of a parallel testing algorithm for serological testing of HIV antibodies in the patient's sera using a combination of three (3) different screening methods, in a stepwise order for the detection of HIV-1 and HIV-2 in the blood [15].

Rapid HIV Screening Test (Screening 1)

HIV screening 1 was performed using Determine HIV-1 and 2 kit (manufactured by Abbot Japan Co Ltd. Tokyo, Japan). The procedure was described by the manufacturer. Briefly, 50 μ l of plasma sample from participants were applied to appropriately labeled sample pads. After 15 minutes of sample application, the results were read. The inherent quality control of the kit validates the results. Two visible red lines occurring in the region labeled control and test represents HIV seropositive reaction while a single red colour in the region of control validates the test kit. Absence of red line in the test region represents HIV seronegative reaction.

Rapid HIV Screening Test (Screening 2)

The HIV screening 2 was carried out using Uni-Gold HIV 1 and 2 test kit (manufactured by Trinity Biotech Plc Co Wicklow Ireland). The procedure was described by the manufacturer.

Two drops (60 μ l) of the plasma sample was added over the sample pad carefully. This was followed by the addition of two drops (60 μ l) of the wash reagent to the sample port. The result as indicated by the appearance of one or two pink/red bars was read 10 minutes after the addition of the wash reagent.

Rapid HIV Screening Test (Screening 3 or Tie Breaker)

The Tie breaker or HIV screening 3 test was performed when the results of the screening I and II was indeterminate (discordant). STAT- PAK HIV 1and 2 assay test kit (manufactured by Chembio diagnostic system INC Newyork, USA). This method utilizes immobilized antigen for the detection of antibodies to HIV 1 and 2 in the human

plasma. The procedure was as described by the manufacturer of the kit. In brief, 50µl of plasma sample was dispensed into appropriately labeled sample wells, then three drops of running buffer was added drop-wise into the appropriately labeled sample wells. The results of the test were read at 10 minutes after the addition of the running buffer. This method had inherent quality control that validates the results. The presence of two pink lines in the region of test sample and control indicates HIV seropositive reaction while a single pink line at the control region indicates HIV seronegative reaction. HIV seropositive results using these two methods were used to confirm participants presenting with HIV infection.

Cytokines quantitation

Plasma levels of the cytokines IL-2 and IFN- γ were measured using the ELISA human IL-2 and IFN- γ immunoassay kits (Nanjing Pars Biochem CO., Ltd, China) according to the manufacturer's instructions and standard operation procedure.

Statistical analysis

Variables were expressed as frequencies and percentage. Statistical analysis was performed using statistical package for social sciences (SPSS) software version 23.0 (SPSS Inc. Chicago, IL, USA, 2020). ANOVA and student t test was used to find the association between two or more variable. *p*-values of less than or equal to 0.05 was considered statistically significant.

Results

Majority of the study groups were male (66.92%) with only (33.08%) female, most of them are married (56.92%) followed by single (29.23%). Majority of the patients in the study group were under the age group of 18-29 (46.67%). Most of them attained secondary school level (46.92%) of education and self-employed (50.00%) (**Table 1**). **Table 3** showed the mean plasma level of IL-2 and IFN- γ in MDR-TB/HIV co-infected treatment-naïve

(group 1a), MDR-TB monoinfected treatment-naïve patients (group 2a), MDR-TB/HIV co-infected treatment-experienced patients (group 1b) and MDR-TB monoinfected treatment-experienced patients (group 2b) were significantly lower ($p < 0.05$) compared with similar value in apparently healthy control (group c). The mean plasma levels of IFN- γ (8.31 ± 3.56 pg/ml) was significantly ($p < 0.041$) higher in MDR-TB/HIV co-infected treatment-naïve patients (group 1a) compared to MDR-TB monoinfected treatment-naïve patients (group 2a) (6.89 ± 2.14 pg/ml). Conversely, the plasma levels of IL-2 (210.02 ± 59.27 pg/ml) in MDR-TB co-infected with HIV treatment-naïve patients (group 1a) were significantly decreased ($p < 0.026$) compared with MDR-TB monoinfected treatment naïve-patients (group 2a) (244.20 ± 108.07 pg/ml) (**Table 4**). We found that there were no statistical different of plasma level of Interleukin-2 and IFN- γ cytokines measured between MDR-TB/HIV co-infected treatment naïve-patients (group 1a) and MDR-TB/HIV co-infected treatment-experienced patients (group 1b) (**Table 5**). The result of mean plasma level of IL-2 and IFN- γ were not observed to show significant differences ($P > 0.05$) between MDR-TB monoinfected treatment-naïve patients (group 2a) and MDR-TB monoinfected treatment-experienced patients (group 2b) (**Table 5**). The result in **table (6)** show that the mean plasma level of IFN- γ (17.37 ± 18.44 pg/ml) were significantly ($p < 0.007$) higher in DS-TB co-infected with HIV treatment-experienced patients (group 3) than the MDR-TB co-infected with HIV treatment-experienced patients (group 1b) (7.99 ± 8.79 pg/ml). The plasma level of IL-2 (381.11 ± 65.61 pg/ml) in DS-TB co-infected with HIV treatment-experienced patients (group 3) was increased compared to MDR-TB co-infected with HIV treatment-experienced patients (group 1b) (183.58 ± 63.71 pg/ml) but not statistically difference.

Table 1. Socio demographic MDR-TB/HIV co-infected group.

Characteristics	Number of Subjects	Percentage (%)
Gender	130	
Male	87	66.92
Female	43	33.08
Age (years)	90	
18 – 29	42	46.67
30 – 49	32	35.56
50≤	16	17.78
Marital Status	130	
Married	74	56.92
Single	38	29.23
Widowed	7	5.38
Divorced	11	8.46
Educational Level	130	
No formal	19	14.62
Primary	27	20.77
Secondary	61	46.92
Tertiary	23	17.69
Employment Status	130	
Civil Service	14	10.77
Self employed	65	50.00
Student	18	13.85
Unemployed	33	25.38

Table 2. Plasma levels of IL-2 and IL-10 in studied groups.

Variables	Group 1a (n=15)	Group 1b (n=15)	Group 2a (n=20)	Group 2b (n=20)	Group 3 (n=20)	Group c (n=40)
IL-2 (pg/ml)	210.02 ± 59.27	183.58 ± 63.71 ^{a1}	244.20 ± 108.07 ^{a2}	212.98 ± 79.90	381.11 ± 65.61	390.80 ± 41.21
IL-IFN-γ (pg/ml)	8.31 ± 3.56 ^{d1}	7.99 ± 8.78 ^{d2}	6.89 ± 2.14 ^{d3}	10.65 ± 10.55	17.37 ± 18.44 ^{d4}	25.46 ± 20.17

Key: Values are mean ± standard deviation; n = number of Subjects; ; MDR-TB = multidrug resistant tuberculosis; DS-TB = drug susceptible tuberculosis; HIV = human immunodeficiency virus; ART= antiretroviral therapy; ATT=anti-tuberculosis therapy; IL-2 = interleukin 2; IFN-γ = interferon-gamma; Significant differences: **a**¹ ($p<0.001$)= Group 1b versus Group 3; **a**² ($p<0.010$)= Group 2a versus Group c; **d**¹ ($p<0.041$)= Group 1a versus Group 2a; ; **d**² ($p<0.020$)= Group 1a versus Group 1b; **d**³ ($p<0.001$)= Group 2a versus Group 2b; **d**⁴ ($p<0.007$)= Group 1b versus Group 3 by Tukey-Kramer Multiple Comparisons Test.

GROUP 1a = MDR-TB co-infected with HIV ATT and ART treatment-naïve patients.

GROUP 1b = MDR-TB co-infected with HIV ATT and ART treatment-experienced patients.

GROUP 2a = MDR-TB ATT treatment naïve patients.

GROUP 2b = MDR-TB ATT treatment-experienced patients

GROUP 3 = DS -TB co-infected with HIV ATT and ART treatment-experienced patients

Group c = apparently healthy control.

Table 3. Effect of HIV on plasma level of IL-2 and IFN- γ on MDR-TB.

Parameter	MDR-TB/HIV (n=15)	MDR-TB (n=15)	p-value
	Treatment-Naïve	Treatment-Naïve	
	Mean \pm SD	Mean \pm SD	
IL-2 (pg/ml)	210.02 \pm 59.27	244.20 \pm 108.07	0.026
INF- γ (pg/ml)	8.31 \pm 3.56	6.89 \pm 2.14	0.041

Key: Values are mean \pm standard deviation; n = number of Subjects; IL-2 = interleukin 2; IFN- γ = interferon-gamma; ART = antiretroviral therapy; ATT = anti-tuberculosis therapy; SD = standard deviation; MDR-TB = multidrug resistant tuberculosis; HIV = human immunodeficiency virus; p-values of less than or equal to 0.05 was considered statistically significant.

MDR-TB/HIV = MDR-TB co-infected with HIV ATT and ART treatment-naïve patients.

MDR-TB = HIV negative MDR-TB ATT and ART treatment-naïve patients.

Table 4. Effect of antiretroviral therapy and anti-TB therapy on IL-2 and IFN- γ .

Variable	MDR-TB/HIV	MDR-TB/HIV	p-value
	Treatment-naïve	Treatment-experienced	
	Mean \pm SD (n=15)	Mean \pm SD (n=15)	
IL-2 (pg/ml)	210.02 \pm 59.27	183.58 \pm 63.71	0.791
IFN- γ (pg/ml)	57.69 \pm 26.85	49.74 \pm 17.56	0.124

KEY: Values are mean \pm standard deviation; n = number of Subjects; SD = standard deviation; IL-2 = interleukin 2; IFN- γ = interferon-gamma; ART=antiretroviral therapy; ATT=anti-tuberculosis therapy; MDR-TB = multidrug resistant tuberculosis; HIV = human immunodeficiency virus; p-values of less than or equal to 0.05 was considered statistically significant.

Table 5. Effect of anti-TB therapy on IL-2 and IL-10.

Variables	MDR-TB	MDR-TB	p-value
	Treatment-naïve	Treatment-experienced	
IL-2 (pg/ml)	244.20 \pm 108.07	212.98 \pm 79.90	0.197
IFN- γ (pg/ml)	6.89 \pm 2.14	10.65 \pm 10.55	0.001

Key: Values are mean \pm standard deviation; n = number of Subjects; IL-2 = interleukin 2; IFN- γ = interferon-gamma; ATT=anti-tuberculosis therapy; MDR-TB = multidrug resistant tuberculosis; p-values of less than or equal to 0.05 was considered statistically significant.

Table 6. Comparison between MDR -TB/HIV and DS -TB/HIV treatment-experienced.

Variable	MDR-TB/HIV	DS-TB/HIV	p-value
	Treatment-experienced	Treatment-experienced	
	Mean \pm SD	Mean \pm SD	
IL-2 (pg/ml)	183.58 \pm 63.71	381.12 \pm 65.61	0.914
IFN- γ (pg/ml)	7.99 \pm 8.79	17.37 \pm 18.44	0.007

Key: Values are mean \pm standard deviation; n = number of Subjects; SD = standard deviation; IL-2 = interleukin 2; IFN- γ = interferon-gamma; ART = antiretroviral therapy; ATT = anti-tuberculosis therapy; MDR-TB = multidrug resistant tuberculosis; DS-TB = drug susceptible tuberculosis; HIV = human immunodeficiency virus; p-values of less than or equal to 0.05 was considered statistically significant.

Figure 1. Plasma levels of IL-2 in group 1a, group 1b, group 2a, group 2b, group 3 and group c. Bars represent mean standard deviation.

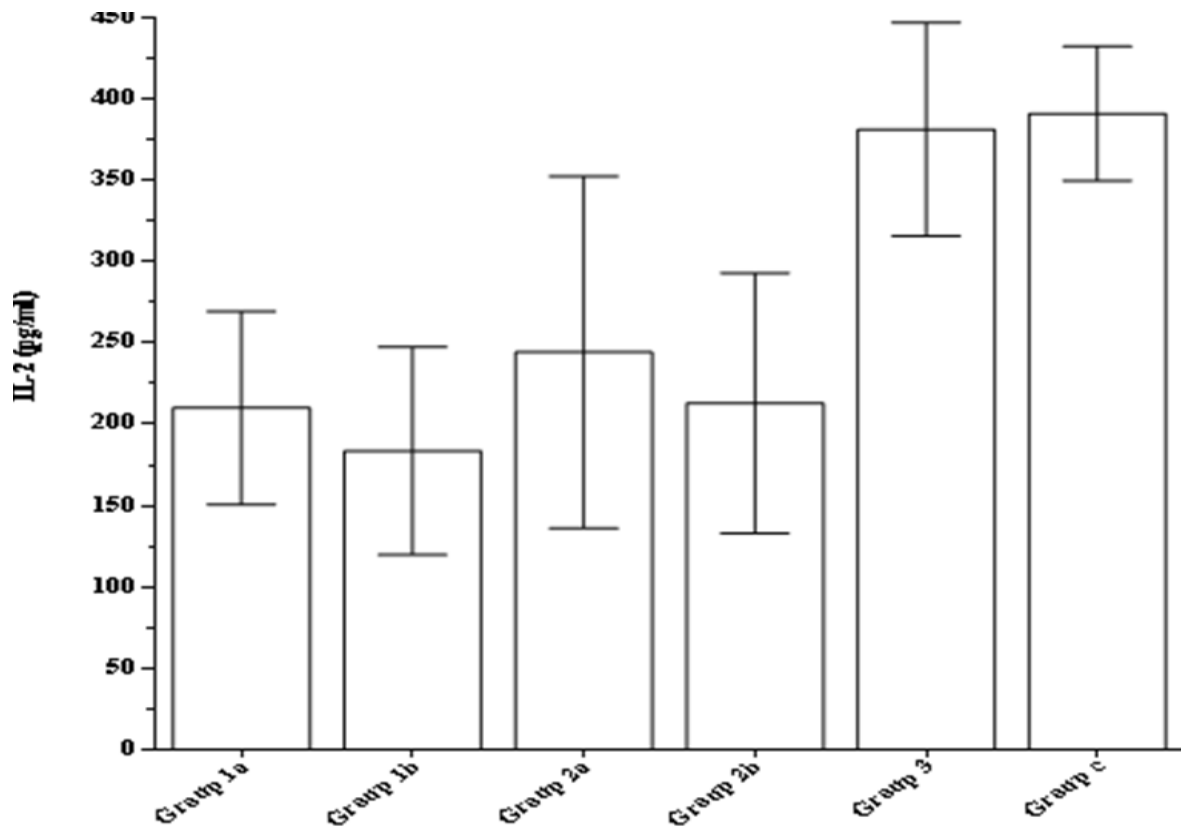
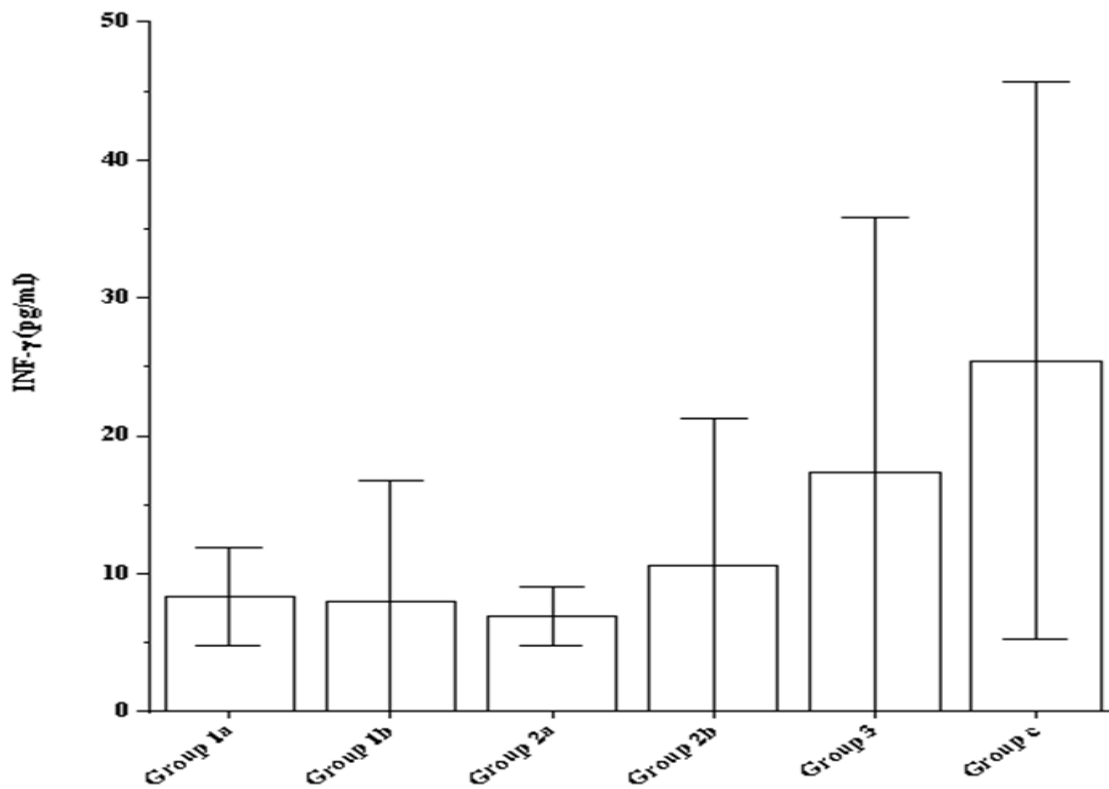


Figure 4.2 Plasma levels of IFN- γ in group 1a, group 1b, group 2a, group 2b, group 3 and group c. Bars represent mean standard deviation.



Discussion

In the current study, the finding of 35.24 ± 1.53 years as mean age for MDR-TB co-infected with HIV patients. These findings are consistent with reports of previous studies **Cherono et al.** [16] who indicated that TB/HIV infection affect reproductive age group of between twenty five to forty five years because these are individuals who are sexually active hence the transmission of HIV is very high. Married had higher proportion (56.92%) of co-infection than single (43.08%) counterpart. These findings are concurred with the finding of **Cherono et al.** [16]. Married couple is at risk of infection when one constituted infidelity. Although patients in all educational levels were prone to multidrug resistant tuberculosis co-infected with HIV. Secondary education had higher proportion (46.92%). This is in contrast to the findings conducted in Zambia by **Muyunda et al.** [17] who reported higher percent among primary school level. It was also in disagreement with the results of the study carried out by other researchers who found that patients with high education level, with high chances of being employed compared to those with unskilled occupations having attained low educational level [17]. Male had higher co-infection (66.92%) than females (33.08%). This is in contrast with the finding of **Akanbi et al.** [14] in Kenya who found higher prevalence of tuberculosis TB/HIV co-infection in females compared to males. Most of them were self-employed (50.00%) followed by unemployed (25.38%). Individuals with low income earning are more predisposed to the MDR-TB co-infected with HIV than those with high income generating and stable jobs.

This study, showed significantly ($p < 0.05$) lower plasma levels of IL-2 in MDR-TB co-infected with HIV treatment-naïve patients, MDR-TB mono-infected treatment naïve-patients, MDR-TB co-infected with HIV treatment-experienced patients, MDR-TB mono-infected treatment-experienced patients and drug susceptible tuberculosis co-infected with HIV treatment-experienced patients compared with apparently healthy control group. Plasma level of Interleukin-2 production among MDR-TB/HIV co-infected treatment-naïve patients was significantly ($p < 0.026$) reduced compared to MDR-TB mono-infected treatment-naïve patients (**Table 3**). This is in consistent with **Nosik et al.** [1] who reported decreased IL-2 among persons with co-infection. This might be due to the depletion of

helper T cells. In this study, the level of IL-2 expression in MDR-TB/HIV co-infected treatment-experienced patients remained almost the same as in MDR-TB/HIV co-infected treatment-naïve patients. This is consistent with the study conducted by **Nosik et al.** [1].

The study shows that, MDR-TB/HIV co-infected treatment-naïve patients, MDR-TB mono-infected treatment-naïve, MDR-TB/HIV co-infected treatment-experienced patients, MDR-TB mono-infected treatment-experienced patients and DS-TB/HIV co-infected treatment-experienced patients had significantly ($p < 0.05$) decreased plasma level of IFN- γ compared to apparently healthy control. This is in contrast with **Nosik et al.** [1] who reported increased plasma level of IFN- γ in all the groups of patients in comparison with the apparently healthy control group. IFN- γ was higher in MDR-TB/HIV co-infected treatment-naïve patients compared to MDR-TB treatment-naïve mono-infected patients but not statistically different. This is in contrast with **Nosik et al.** [1] who reported significantly reduced plasma level of IFN- γ in patients with TB/HIV co-infection compared to TB mono-infected patients. IFN- γ in MDR-TB/HIV co-infected treatment-naïve patients was significantly higher compared with MDR-TB/HIV co-infected treatment-experienced patients. This may be due to fewer CD4+ T cells that can produce IFN- γ [18]. The level of cytokines (IL-2 and IFN- γ) expression in MDR-TB/HIV co-infected treatment-naïve patients and MDR-TB/HIV co-infected treatment-experienced patients remained almost the same. This is in agreement with **Nosik et al.** [1].

Conclusion

The syndemic interaction between the HIV and MDR-TB epidemics has had deadly consequences in Nigeria and yet, to the best of our knowledge, this study is the first to directly compare plasma levels of IL-2 and IFN- γ in MDR-TB/HIV co-infected patients and MDR-TB mono-infected patients in the country. Our study revealed significantly reduced plasma level of IL-2 in MDR-TB and HIV co-infected patients compared with MDR-TB mono-infected subjects, suggesting a more advanced immunodeficiency in co-infected patients. Several studies have reported an association of TB with the acceleration of immunodeficiency and increased virus replication in HIV infection.

Recommendation

Based on the findings from this study, it is recommended that: Our study was case control; further studies should be conducted to include larger sample size. Recombinant human interferon gamma interleukin 2 (IL-2) should be used to improve immunity status among MDR-TB/HIV co-infected patients.

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Conflict of interest

There are no conflicts of interest.

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Abbreviations

AKTH	= Aminu Kano teaching Hospital
ATT	= Anti tuberculosis therapy
ART	= Antiretroviral therapy
CD4 cell	= Cluster of differentiation type 4
DS-TB	= Drug susceptible tuberculosis
EDTA	= Ethylene diamine tetra acetic acid
ELISA	= Enzyme-linked immunosorbant assay
HIV	= Human immunodeficiency virus
IL-2	= Interleukin-2
IL-2R	= Interleukin-2 receptor
IFN- γ	= Interferon-gamma
MDR-TB	= Multidrug resistant tuberculosis
MBT	= <i>Mycobacterium tuberculosis</i>
ml	= Milliliter
NK cell	= Natural killer cell
n	= Number of subject
pg/ml	= Picogram per milliliter
RIF	= Rifampicin
rpm	= Revolution per minute
SD	= Standard deviation
SPSS	= Statistical Package for Social Sciences
PCR	= Polymerase chain reaction

TB	= Tuberculosis
Th 1 cell	= T helper 1 cell
Tc	= Cytotoxic T cell
TNF- α	= Tumor Necrosis Factor-alpha
WHO	= World health organization

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