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Associationbetween Gender Differences And Cd4 immunological Failure Among Human Immunodeficiency Virus Treatment Naïve Patients On Antiretroviral Therapy Atitezhi-Tezhi District Hospital.

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Abstract

Objectives:TodescribeCD4immunologicalfailureinmaleandfemaleHIVtreatmentnaïvepatientsonHAARTatItezhitezhidistrictHospital.Toachievethisobjectivethestudywasaimedat identifyingandcomparingCD4immunologicalfailurebetweenmaleandfemale HIVtreatmentnaïvepatientsonantiretroviraltherapy.

StudyMethod: Adescriptivecross-sectionstudy wasemployed to collect secondary data from patient files. Data collected was serum CD4 cell count at baseline of ART enrolment and at Six (6) months of treatment. Theunitanalysiswereadulttreatmentnaïvepatientsatleastsixmonthsonantiretroviraltherapy at Itezhi-tezhi District Hospital inCentral Province of Zambia. A probability Simple random methodofsampling wasusedtopickfilesofparticipants.Thefileswerefirstenteredonexcelspreadsheet,allocatedarandomnumberandrandomized.Thereafter,thefirst246files will beselected and used in this study.

Results: As of June 2015, the cumulative ever on ART at Itezhi- tezhi district was 4073 and out of this figure 1465 (36%) had died, migrated or lost to follow. Currently, there were only 2508 on ART and out of this figure a higher population was that of adult female. Using Pearson Chi square test, it was found thatdifferences in gender were significantly associated with CD4 immunological failure and men were more vulnerable.

Conclusion; Men on ART were found to have a higher prevalence of CD4 immunological failure compared to women, regardless of their baseline, Age, weight and CD4 count. However, additional studies are needed to confirm men`s susceptibility to treatment failure by incorporating virological and clinical monitoring in these studies.

Key words: *Adherence, CD4 Immunological failure, treatment naïve patients, antiretroviral therapy*

I. INTRODUCTION

According to the World Health Organization (WHO), there has been an increase in the number of people receiving antiretroviral therapy worldwide. In addition, over 6.6 million (representing a 16 times increase) patients on treatment as of 2010 (Estill J et al., 2013; Cornell M et al, 2011; E). Despite this increase in access to HIV treatment(Ferradini et al., 2006), many patients are experiencing treatment failure: for example, 97/105 (92%) patients in Asiaharboured≥1 resistance –associated mutations at first line failure(Jiamsakul et al., 2014). Similar studies conducted in Zambia, found an increase from 3% in 2011 to 11 % in 2013 in the cases of morbidity, mortality, resistant associated mutations (RAM) and in patients switching to second and third line therapy (Price et al., 2011; Thomas et al., 2013). Thus, this increase in treatment failure is posing a challenge in the management of antiretroviral therapy (ART) programs and as a result recommendations have been made to quickly detect and control it (Ferrandini et al., 2006; WHO, 2010, Cornell M et al., 2011; Price M. et al., 2011; Estill J et al., 2013; Thomas et al., 2013; Jiamasakul, 2014).

CD4 immunological failure is an essential monitoring parameter in the detection of HIV treatment failure. CD4 immunological failure has resulted in high levels of mortality and morbidityof ART patients and in an increase in the need for more expensive second and third line drug regimen thus raising the cost of running ART programs (WHO, Progress report, 2010; KihulyaMageda et al., 2012; Estill J wt at., 2013). Furthermore,

it is currently known that men tend to start ART at much more advanced stage of HIV disease compared to women reason being that men are rarely tested for HIV and as such are unaware of their status(Laurent C et al., 2013) making them more disadvantaged in accessing treatment and appear vulnerable to treatment failure compared to women(Penot P et al., 2014).

Regardless of the knowledge of men accessing treatment late(Laurent C et al., 2013), it is unknown whether this can translate into them failing there treatment and as such the association between gender and CD4 immunological failure is still uncertain(Penot P et al., 2014).

Nonetheless, a number of researchers have recommended for further studies be conducted in order to contribute to the knowledge of HIV treatment and identify the main cause of treatment failure. Recommendations that have been made include; (i) comparing the effectiveness of ART regimen(Chi et al., 2009) and (ii) confirming the poor prognosis of men on ART(Penot P et al., 2014). This study aimed at answering the second recommendation.

II. METHODOLOGY

This chapter will address the data and methods together with procedures to be used in addressing the research objectives. It will further describe the study site, study population, sample size, sampling technique, procedure, data to be collected and data analysis.

2.1 Study design

I employed a cross sectional study(Cresswell J, 2003) on ART treatment naïve patients at least six months on ART to collect primary data from existing patient files at the ART Clinic. This was because the study objectives require the prevalence of immunological failure to be assessed at one point time which was at 24 weeks after ART initiation.

2.2 Study Population

The unit analysis was adult treatment naïve patients at least six months on treatment with antiretroviral drugs.

2.3Study site

The study was conducted at Itezhi-tezhi District-Hospital ART Clinic in Central Province of Zambia.

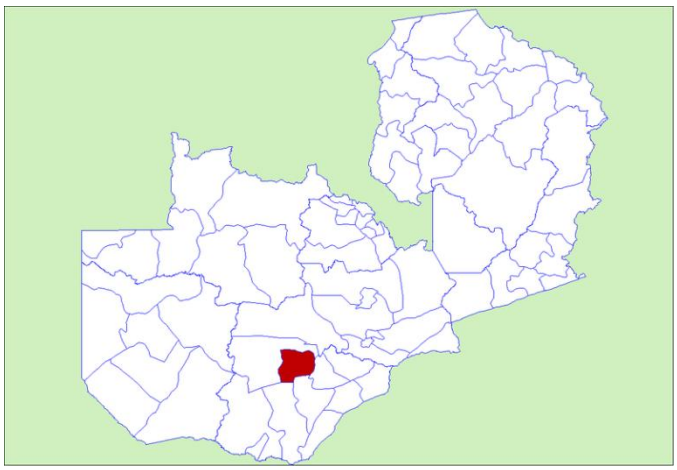

Figure 2; shows the location of Itezhitezhi district in Zambia.

2.4Sample size

Based on the expected 20% attritional prevalence of HIV treatment failure in Sub-Saharan Africa for patient's ≥ 5 years on ART in Zambia(Thomas et al., 2013), 246 patients` files were reviewed in order to identify the true prevalence with precision of +/-5% and 95% confidence interval.

$$N = \frac{Z^2 \times P(1-P)}{d^2} = \frac{1.96^2 \times 0.2(1-0.2)}{(0.05)^2} = 246$$

P= HIV attritional prevalence (20%), d= standard error (5%), N = sample size & Z= Z-score (1. 96) (Formula adopted from Fisher, 2003).

2.5Sampling technique

A probability Simple random method of sampling was used to pick files of participants. All files meeting the inclusion criteria for the study was subjected to a simple random sampling procedure using excel data

base. The files were first entered on excel spread sheet, allocated a random number and randomized. Thereafter, the first 246 files were selected to be included in the study.

2.6 Inclusion criteria

Only adult male and female ART adherent participants above the age of 16 years were included in the study. Additionally, only participants who have been on treatment for at least six months at the time the assessment was conducted were included in the study.

2.7 Exclusion criteria

In the study participants below the age of 16 years and those participants on therapies that may interfere with serum CD4 count such as patients receiving long term cancer chemotherapy and corticosteroid treatment or any other immunosuppressive therapy at baseline of ART initiation were excluded. This was in order to minimize cofounders to serum CD4 count.

2.8 Procedure

The monitoring parameter for the study was the serum CD4 cell count from the patient`s files. From each file, the baseline CD4 count at 6-months was captured and recorded on the data sheet. The data was then entered on the SPSS version 16.0 for analysis to find prevalence in the two groups of gender. The prevalence in both gender groups was then tested using chi square test to find the association that gender differences has on CD4 immunological failure.

2.8.1 Data Collection

The data that was collected in order to answer the research questions included; Age of patients, Gender, baseline CD4 count, CD4 count at 6months and baseline body mass index.

This data was collected using a datasheet which was adopted from Chi et al., (2009), though modified to meet the design of the study (Appendix 1).

2.8.2 Variables

Variables used to identify CD4 immunological failure and demographic variables were used to find the research objectives (table 1).

2.9 Ethical Consideration

The study commenced only after receipt of approval and clearance from National ethics committee, LAMU-Faculty of Pharmacy and dietetics and Itezhitezhi District Medical office. Patient confidentiality was high adhered to and raw data was secured to prevent an authorized access. The raw data was only stored for six weeks after submit ion of final report.

Table 1; Operational variables, their definitions and Scale of measurement

	Variables	Definition	Scale
	Age	At Birthday	Continuous
	Gender	Male and female	Dichotomous
	Baseline CD4 count	CD4 count at ART initiation	Continuous
	Baseline body mass index (BMI)	BMI at ART initiation	Continuous
	CD4 Immunological failure	Serum CD4 cell count 24 weeks after initiating ART	Ordinal
	Association between gender differences and CD4 Immunological failure	Total numbers of males and females presenting with CD4 Immunological failure	Categorical

3. 10 Data management

Raw data collected was be transformed to numeric values (Appendix II) which were then entered on SPSS version 16.0 for analysis.

3.11 Data analysis and interpretation

Chi square test was used to find the difference between male and female HIV treatment naïve patients who develop CD4 immunological failure (Table 2).

Table 2: Variables and their descriptive analysis methods

NO	Variables	Descriptive Analysis	Figure Analysis	Statistical Analysis
	Age	Mean, Mode & SD	Frequency table	N/A
	Gender	Percentage	Pie chart	N/A
	CD4 Immunological failure in each group	Prevalence	Bar Chart	N/A
	Baseline CD4 count	Mean, Mode & SD	Frequency table	N/A
	Baseline body mass index (BMI)	Mean, Mode & SD	Frequency table	N/A
	associated of gender differences and CD4 Immunological failure	Cross tabulation	Table	Correlation

III. RESULTS

The results in this section have been presented according to the specific objectives of the study;

3.1 Demographic Characteristics of study participants

As of June 2015, the cumulative ever on ART at Itezhi- tezhi district was 4073 and out of this figure (36%) 1465 had died, migrated or lost to follow. Currently, there were only 2508 on ART and out of this figure a higher populations was that of female aged above 15 years (Figure 3).

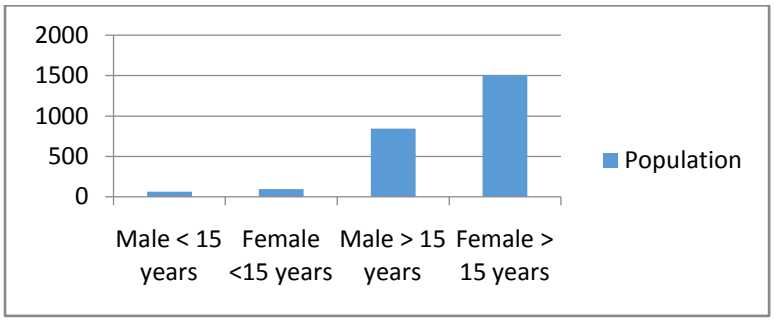

Figure 3; Distribution of patients on ART at Itezhi-tezhi as of June 2015

Amongst the eligible files, 246 were selected to be included in the study. From the list of participants, it was identified that a higher population was that of female (Figure 4).

In addition, the study shows that a larger population of study participants was married and statistics indicate that there was a high illiteracy level among women who also happened to have a low monthly household income (Table 3). Furthermore the means for the baseline body mass index (BMI), baseline CD4 count and CD4 count after six months of ART were found to be lower in men compared to women.

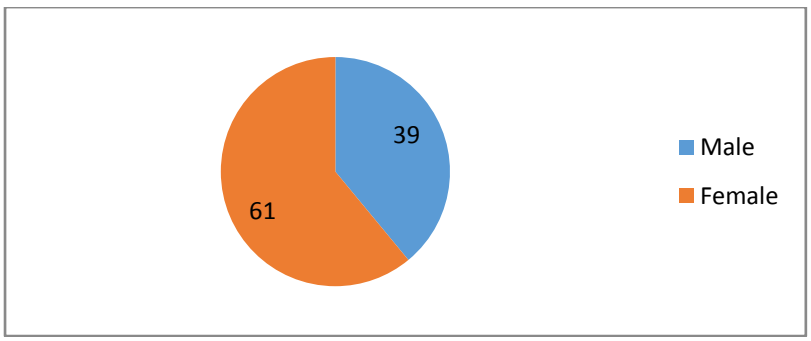

Figure 4; Percentage of study participants by gender

Table 3; ART Patients` Demographic Characteristics by gender

	Men	Women
NO. Of participants	96 (39.0%)	150 (61.0%)
Mean Age (years)	42.8	37.1
Marital status		
Single	12 (41.4%)	17 (58.6%)
Married	63 (42.9%)	84 (57.1%)
Divorced	13 (35.1)	24 (64.9%)
Widowed	5 (21.7)	18 (78.3%)
Separated	3 (30.0%)	7 (70.0%)
Level of education		
Never been to school	6 (24.0%)	19 (76.0%)
Basic Education	49 (38.6%)	78 (61.4%)
Secondary education	34 (40.5%)	50 (59.5%)
College/ University	7 (70.0%)	3 (30.0%)
Occupation		
Unemployed	8 (28.6%)	20 (71.4%)
Employed	25 (65.8%)	13 (34.2%)
Attending school	0 (0.00%)	6 (100%)
Housewife	0 (0.00%	31 (100%)
Any other	63 (44.1%)	80 (55,9)
Participants Monthly Household Income		
K 500 and below	31 (25.8%)	89 (74.2%)
K500-K1000	22 (37.3%)	37 (62.7%)
K1000-K2000	28 (63.6%)	16 (36.4%)
Above K2000	15 (65.2%)	8 (34.8%)
Mean Body weight	59.67	53.31
Mean BMI	20.92	21.96
Mean Baseline CD4	208.8	277.1
Mean CD4 after 6 months	257.8	388.1

Note: Demographic characteristic are patients characteristics at initiation of ART

3.2 Prevalence of CD4 immunological failure in male and female treatment naïve patients after 24 weeks on ART

In this study, it was found that the prevalence of CD4 immunological failure was higher in men (52.9%) compared to women (47.1%) regardless of their baseline characteristics (Figure 5) and the overall prevalence of CD4 immunological failure was found to be 35% (Table 10).

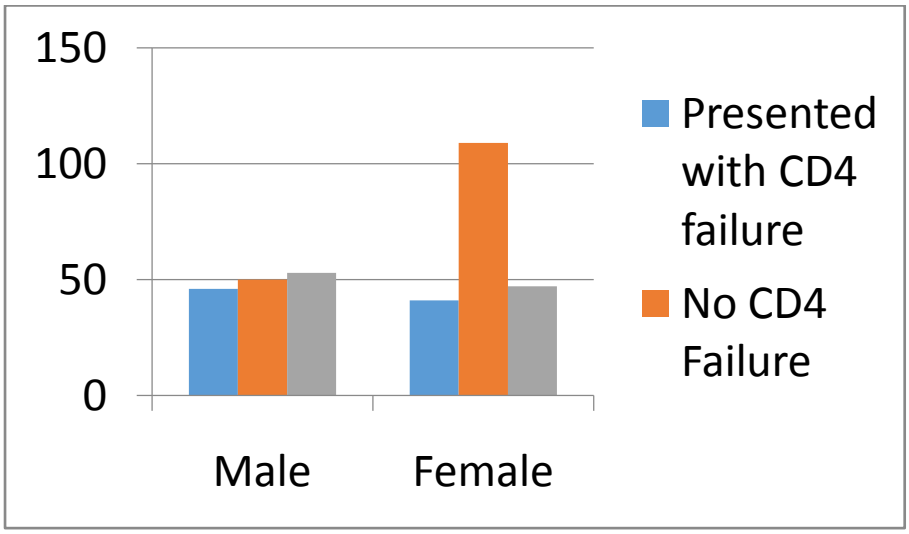

Figure 5: Distribution of the 246 study participants and % CD4 immunological failure among treatment naïve patients

3.3 Association between Gender and CD4 Immunological failure

Using Pearson Chi square test, it was found that gender was significantly associated with CD4 immunological failure (Table 4). In male gender was more allied to experience CD4 immunological failure regardless of their baseline characteristic (Figure 5).

Table 4; Chi-Square to tests association between gender and CD4 immunological failure

	Value	Df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	10.850[a]	1	.001		
Continuity Correction	9.968	1	.002		
Likelihood Ratio	10.762	1	.001		
Fisher's Exact Test				.002	.001
Linear-by-Linear Association	10.805	1	.001		
N of Valid Cases[b]	246				
a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 33.95.					
b. Computed only for a 2x2 table					

Note; Study is significant when P-Value is less than 0.05

IV. DISCUSSION

Discussion

This study shows that male gender is significantly associated with CD4 immunological failure (P-value =0.002 by Pearson Chi-Square Test) with men experiencing a higher prevalence than women (Figure 5). The Evidence that gender differences is associated with CD4 immunological failure has been found to exist regardless of the patient's baseline characteristics such as age, BMI, CD4 count, level of education, marital and economic status. The findings of this study coincide with other similar studies. In particular, the finding of this study is in consistence with a study conducted in Bukina Faso which found that men were more vulnerable to virological failure (Penot et al., 2014). The gender differences in prevalence of CD4 immunological failure observed in this study may be explained in relation to gender differences in pharmacokinetic and pharmacodynamic profile of antiretroviral drugs and in adherence levels ((Gandhi M. et al., 2004); (Ofotokun I. et al., 2007)). With

regards to the earlier statement, higher concentrations of antiretroviral drugs have been observed in women than in men(Marzolini C et al., 2001). These higher concentrations of drugs observed in women may be due to the enzyme inhibition process of estrogen while lower concentration observed in men may be due to enzyme induction of testosterone during metabolic process (Veldkamp AI et al., 2001). Secondly, men have generally been associated with poor adherence to ART compared to women(Bastard M. et al, 2011).

On the contrary, other authors in Africa tend to disagreeand have since stated that it is unfair to treat the male gender as failing treatment because most ART-programs and policies are blind to the treatment needs of men as they are not granted equal access to ART(Morna Cornell et al., 2011). Equally, authors in South Africa attributed the differences in mortality between men and womento background differences in mortality unrelated to HIV/AIDS epidemic(Cornell M et al., 2012). Despite these contradictory facts, it is interesting to note that according to literature surveyed, there has been no study that has found a higher prevalence of CD4 immunological failure in women. Regardless of the above explanations for associating men to having a higher prevalence of CD4 immunological failure this study had several limitations; firstly, the findings might not be fully generalized to represent the national picture as it was only conducted at one ART site in Zambia. Regardless of this, I am fully confident that the findings at this site could be a reflection of other sites in Zambia although this assumption needs to be confirmed.Secondly, due to limited time available for data collection, a cross section study was employed, a prospective cohort study could have presented with a higher power to detect the difference in CD4 immunological failure observed.

Finally, I did not look at the reasons as to why there were these gender differences in treatment prognosis and did not conduct therapeutic drug monitoring to determine serum concentrations of antiretroviral drugs.

V. CONCLUSION

In conclusion, men on ART were found to have a higher prevalence of CD4 immunological failure than women, regardless of their baseline HIV disease stage, Age, weight and CD4 count. However, additional studies are needed to confirm men`s vulnerability to treatment failure by incorporating virological and clinical monitoring in future studies. Determining the causes for men having a higher CD4 immunological failure may also help improve their treatment prognosis. The findings in this study calls for additional efforts to be put in place in order to support the adherence of men on ART at itezhi-tezhi District Hospital.

Conflicts of interests

There were no perceived conflict of interest and as such the study progressed smoothly

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