RESEARCH PAPER

The effects of gender on clinical and immunological response to antiretroviral therapy among people living with HIV in Ile-Ife, Nigeria

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Abstract

Introduction: Gender may influence treatment outcome in people living with human immunodeficiency virus (HIV). This study aimed to determine the role of gender in the clinical and immunological responses of patients on antiretroviral therapy (ART).

Material and methods: Two hundred and twenty-seven patients from the Virology Research Clinic, of the Obafemi Awolowo University Teaching Hospital, Ile-Ife, Nigeria had their records retrieved. These were retrospectively analyzed to assess the clinical and immunological responses to therapy at commencement of ART and every 6 months thereafter for 2 consecutive years.

Results: Females account for 67.8% of the subjects. Mean ages at initiation of ART for males and females were 42.47 and 36.27 years, respectively. Prior to the initiation of ART, the mean body mass index (BMI) in males (21.26) was slightly higher than that of females (20.94), while the CD4 cell count was higher in females (198 cells/μl) than in males (183 cells/μl). The differences in the mean BMI between the genders were not significant after the first (p = 0.09) and second (p = 0.18) year of treatment. The mean CD4 cell counts after the first and second year were 336 and 434 cells/μl in males and 427 and 544 cells/μl in females, respectively. The differences between both genders were significant with a p-value of 0.000 and 0.003 for the first and second year.

Conclusions: Antiretroviral therapy has improved the outlook of people living with HIV. In comparison with the male counterparts, this study found that the female gender gives a better complement to outcome derived from ART.

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Key words: HIV, gender, HAART, immune response.

Introduction

Access to antiretroviral therapy (ART) has been on the increase in Nigeria as in many developing countries. This has impacted significantly on the outlook of people living with human immunodeficiency virus (HIV), transforming HIV infection from acutely fatal disease to a chronic medical condition [1-5]. The CD4 count level for the initiation of highly active antiretroviral therapy (HAART) in Nigeria has been raised from 350 cell/μl to 500 cell/μl and currently, the initiation of HAART in all patients regardless of the CD4 level has been approved. Further improvement in treatment

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outcome is expected in Nigeria as more patients are placed on HAART. Gender has been reported in the past to influence the transmissibility and outcome of HIV [6]. While it may be contentious that the effect of gender on treatment outcome is due to differences in the constitutional make-up of the male and female gender, exogenous factors such as culturally ascribed roles for males and females may significantly influence the outcome in people living with HIV.

The people of South Western Nigeria and Ile-Ife in particular are culturally distinct from the regions where previous work had been done on this subject, and hence the need to examine the role of gender on treatment outcome among people living with HIV in Ile-Ife, Nigeria. The study assesses the effect gender on clinical and immunological responses of HIV patients with comparable CD4 count set point and WHO clinical stage at the commencement of HAART.

Material and methods

Study location

The study was conducted at the Virologic Research Clinic of Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife. It has 650 beds and located at South West geopolitical zone of Nigeria, where it serves patients population referred from various parts. The Virologic Research Clinic of the hospital provides care to over 2,500 patients living with HIV.

Study design

This was a retrospective study, and it reviewed 227 case notes of HIV-positive patients who were 18 years and above, and whose CD4 count was less than 350 cell/µl at the start of HAART or who are in WHO clinical stage 4. The patients reviewed were those on the first line of antiretroviral (ARV) regimen, who were initiated into standard public sector first-line ART regime between January 2006 and January 2013. Public sector regimens include zidovudine (AZT) with lamivudine (3TC) and either efavirenz (EFV) or nevirapine (NVP), Truvada (tenofovir + emtricitabine) with efavirenz or nevirapine, and lastly tenofovir + lamivudine with efavirenz or nevirapine. Other criteria for inclusion are documented adherence more than 95%.

The criteria for exclusion from the study include age less than 18 years, pregnancy within the first two years of initiating HAART, patients less than two years on HAART during the review period, and patients on second line of antiretroviral drugs. The second line regimen is any combination that includes protease inhibitor.

Sampling method and sample size determination

A non-probability sampling was done where patients who met the inclusion criteria were consecutively recruited for the study. The sample size was determined using the Cochran's formula [7]. HIV prevalence of 5.6%, being the highest regional prevalence observed in one of the states within the zone was used in calculating the sample size [8].

n = the desired sample size

$$= \frac{z^2pq}{d^2}$$

P = the proportion in the target population estimated to have a particular characteristic (in this case 0.056)

Z = the standard normal deviation (using 95% confidence level = 1.96)

d = degree of accuracy desired, set at 0.06/2 = 0.03

q = 1.0 – P = 1.0 – 0.056 = 0.944

$$n = \frac{(1.96)\ (1.96)\ x\ (0.056)\ x\ (0.944)}{0.03^2}$$

n = 225.65

Rounded up to 227

Data collection

Relevant data were collected with the aid of proforma from the patients' records. Demographic and baseline characteristics were obtained including gender, age, marital status, body mass index at initiation of HAART and after the first and second year, respectively. The CD4 cell count at initiation of HAART, and after the first and second year were respectively noted. The HAART regimen as well as the duration were also recorded. CD4 counts results were obtained during one of the follow-up visits (months 3, 6, 12, 18, and 24). When the CD4 count was not available for a scheduled follow-up visit, an alternative CD4 count within 2 months of the scheduled visit time window was used for the analysis. The virological outcome of treatment could not be determined due to lack of facility to carry out HIV viral load measurement during the review period.

Statistical analysis

Data were analyzed using SPSS version 16. Differences in clinical and immunological responses between the genders were analyzed using the paired sample correlation, independent *t*-test and test of ANOVA. The criterion for significance for all analysis was a 2-sided *p*-value of less than 0.05 and confidence interval of 95%. We compared the differences in BMI at initiation of HAART, and after the first and second year in males and females. We also compared the differences in the CD4 cell counts between males and females at initiation of HAART and in the first and second year.

Ethical consideration

This analysis was approved by the Director of the Virology Research Clinic, Obafemi Awolowo University Teaching

Hospital Complex, Ile-Ife, Osun State, Nigeria. Individual informed consent was waived because this analysis used currently existing data collected during the course of routine treatment and care, and the data were reported in aggregate without using of individual identifying information.

Results

Socio demographic characteristics

A total of 227 HIV-positive patients were recruited in this study, with females accounting for 67.8% (154) of the subjects. The mean age of initiation of HAART in females was 36.27 years and 42.47 years in males (Table 1). The difference in age between females and males was statistically significant with *p*-value of 0.000. Higher proportions of the patients 183 (80.62%) were married, 25 (11.01%) were widows or widowers, 17 (7.49%) were singles, and the minority 2 (0.9%) were divorced.

Clinical and immunological characteristics at the start of antiretroviral therapy

The mean BMI at initiation of HAART was slightly higher in males (21.26) than females (20.94). This is probably due to the physiologically higher BMI in males. Both males and females commenced ART at WHO clinical stage 4; however, females had a higher mean CD4 count of 198 cells/μl compared to males with mean CD4 count of 183 cells/μl. The differences in means at initiation of HAART between males and females were not statistically significant, with a *p*-value of 0.057 and 0.447 for the BMI and CD4 cell count, respectively.

Treatment response as disease progressed

Following two years of treatment with HAART, the difference in the mean BMI between males and females were not statistically significant after the first ($p = 0.09$) and second ($p = 0.18$) year on treatment (Table 1). Immunological responses however show a different pattern with enhanced and statistically significant response in the females after the first ($p = 0.000$) and the second ($p = 0.003$) year on treatment (Table 1).

Discussion

In Nigeria, women are routinely screened for HIV infection during antenatal clinic care. Mothers of infected children are also frequently screened and subsequently enrolled into care if found to be HIV-positive. The preferential access to screening available to women account for the higher proportions of women enrolled in HIV care. This was further depicted by our study, where high proportions of the 227 patients were females. Higher prevalence of HIV infections observed among women in the developing countries also contributes to the disparity observed in this study. Gender can influence causation and treatment outcome in patients with HIV infection and acquired immunodeficiency syndrome (AIDS). Among the factors that may increase the risk of acquiring the infection in women is the larger surface of the genital mucosa [9].

In developing country like Nigeria, social and empowerment-related factors also play significant role in placing women at risk of acquiring HIV infection. Treatment outcome in patients with HIV may be affected by a number of gender related factors such as sociocultural, behavioral, body size and composition, genetic biochemical factors, and hormonal or reproductive influence [10]. These factors by altering the pharmacologic properties (pharmacodynamic and pharmaco-kinetics) of the drugs may influence treatment outcome in patients with HIV infection [11].

Studies to evaluate the impact of gender on treatment outcome in patients on HAART have been done in the past, with some studies favoring a better clinical outcome and rising CD4 count in women, while some other studies show that men have a better outcome [6, 12-19]. Some other studies do not present significant change in both clinical and immunologic outcome [12, 20, 21]. In addition to the gender-related factors outlines above, the discrepancies in outcome may also be accounted for by the baseline clinical and immunological status of the subject before commencement of ARV [22].

Table 1. Demographic, clinical, and immunological characteristics of patients on antiretroviral therapy

Factor	Males	Females	*p*-value
Frequency	73 (32.2%)	154 (67.8%)	
Mean age	42.47	36.27	0.000
BMI – initial	21.26	20.94	0.057
BMI – first year	20.93	23.23	0.090
BMI – second year	23.12	23.39	0.180
CD4 – initial	183	198	0.447
CD4 – first year	336	427	0.000
CD4 – second year	434	544	0.003

Routine screening for HIV infection in healthy pregnant women is carried out in Nigeria as a part of effort to prevent maternal to child transmission of infection. This practice facilitates the early identification and enrolment of patients whose immunological and clinical status are relatively intact. The females therefore have a relatively higher CD4 count than men at point of enrolment and apparently better treatment outlook as observed in this study.

The women were also observed in this study to present at earlier age than their male counterpart. Similar social economic factors accounting for higher number of females' enrolment may also explain this. The difference in age was statistically significant, thereby affirming the likelihood that men will present at higher age group. However, the mean age in women (36.27 yrs) and the mean age in men (42.47 yrs) were within the young age group, thereby reducing the physiological changes associated with age that might have influence the clinical and immunological outcome of treatment.

The difference in BMI at the first and second year after commencement of HAART was not significantly influenced by gender as observed in this study. This may be because the baseline BMI noted in the study was within normal range. It is therefore expected that during the treatment, patient will return to usual pre-infection BMI rather than increase the weight in the absence of other factors such as excessive eating, diabetic mellitus, and sedentary life styles, which can independently cause weight gain. In study by Stringer et al., higher mortality in patients with BMI less than 16 kg/m^2 is reported [23].

Immunological response as measured by the CD4 count was significantly influenced by gender, with females having better outcome. Similar results were reported in previous studies [7-11]. Gender related factors such as genetic, biochemical molecular, and hormonal factors may account for the observed [20]. Although this study was carried out in a resource limited setting, the introduction of viral load in the evaluation of these patients and the use of resistant testing, thus elimination of resistant drugs usage in the regimen should be investigated in future studies to evaluate gender as a factor that may play an important role in patients' response to HAART.

Conclusions

The outlook of people living with HIV has improved significantly with introduction of HAART. However, the success achieved by these drugs has been plagued by factors such adherence, drug-drug interaction, clinical and immunological status at the start of treatment. While efforts to eliminate these factors are being introduced into clinical practice, the influence of gender has been of increased concern, and this study found that women have a better outcome compared to their male counterparts. Nevertheless, the inclusion of virological assessment and resistant testing are suggested in future studies to further define the influence of gender on HIV treatment outcome in resource limited setting like Nigeria.

Limitation

Resistance testing, although desired, were not done before initiation of HAART. This may influence the type of antiretroviral regimen prescribed, and contributed to the clinical and immunological response regardless of gender.

Conflict of interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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