THE SENSITIVITY AND SPECIFICITY OF WHO CLINICAL STAGING IN PREDICTING CD4 CELL COUNTS IN HIV INFECTED PATIENTS AT THE POLICE HOSPITAL IN ACCRA, GHANA

Otu-Nyarko S[1, 2], Asabilla Baba E [2, 3]

[1]Faculty of Public Health, Ghana College of Physicians and Surgeons, [2]Public Health Department, Ghana Police Hospital, Accra, [3]Mount Crest School of Public Health, Accra

Abstract

Introduction : Initiating an HIV positive client on ART is an important step in the care of PLHIV. Due to a shortage of CD4 machines and reagents, the WHO clinical staging guideline is widely used to determine when to initiate ART in developing countries.

Objective : To determine whether WHO clinical staging is predictive of CD4 of 350 in initiation of ART in patients presenting at the Police Hospital ART clinic.

Methods : We reviewed the records of clients on ART, from 2010 to 2012 and compared the WHO clinical staging and CD4 counts at their first visit to the clinic. Pregnant women, hepatitis B infected patients and children below fifteen were excluded from the study.

Results : Two hundred and five PLHIVs were eligible for inclusion in the study. Sensitivity of the WHO Clinical staging to predict initiation of ART was 44% and specificity 87%. Positive predictive power was 83% and Negative predictive power was 51%.

Conclusion : Almost 50% of those needing ART as per CD4 count were classified as WHO stage 1 or 2. This means that about half of those deemed not qualified to start ART by WHO clinical staging actually needed to be initiated on ART. Access to CD4 machines and reagents must be increased to minimize delay in start of treatment for patients.

Keywords : ART, WHO staging, CD4, PLHIV, specificity and sensitivity

Introduction

The first case of HIV was discovered in Ghana in 1986[1]. As at the end of 2013, Ghana had cumulatively enrolled a total of 84,169 persons living with HIV (PLHIV) on antiretroviral therapy (ART). However, a total of 75,762 PLHIV were alive and on ART medication[2]. Again by the end of 2013, one hundred and seventy-five health facilities including 17 private ones were providing ART services[3]. Police Hospital started an ART clinic in 2008, after training of healthcare workers in management of opportunistic infections and antiretroviral therapy which was organized by the National Aids Control Programme (NACP) in 2007.

Since the early days of HIV infection and AIDS, it has been recognized that the disease progresses in several stages due to the progression of immunosuppression. The level of immunosuppression is linked directly to the CD4 cell count[4, 5, 6].

The World Health Organization (WHO) developed guidelines for such situations where clinical manifestations are presumed indicative of the progression of the disease. Such guidelines are based upon established correlations between CD4 cell count and clinical manifestations. The reliability of these established correlations for the African population, particularly those that are poor, has been questioned in literature.

In many Sub-Saharan countries, CD4 cell count is not widely available or consistently used and instead the WHO clinical staging system is used to determine ART eligibility[7]. However concerns have been raised regarding its discriminatory ability to identify patients eligible to start ART[8]. Where the CD4 count machines are available, frequent stock out of reagents means that clinicians are forced to rely on the WHO clinical classification to initiate ART to patients.

The WHO classification has four clinical stages, numbered stage 1 to stage 4. The clinical stages are hierarchical with standardized clinical parameters; stage 1 is primary HIV infection, while individuals in stage 4 have advanced HIV disease or AIDS. Stage-defining conditions are used to classify patients into one of the four clinical stages[9]. These categories apply to adults and adolescents 15 years-of-age and older. A modified version of the WHO Clinical Staging System is available for infants and children under fifteen years of age[10]. The WHO recommends that HIV-positive adults with CD4 cell count ≤500 cells/mm3 initiate ART. In Ghana, an HIV positive adult qualifies to be put on ART when his CD4 cell count is ≤ 350 or is in WHO clinical stage 3 or 4. If a person is in stage 1 or 2 but the CD4 cell count is ≤ 350, ART is still initiated. Other categories of patients that are started on ART irrespective of CD4 cell counts are pregnant women and patients with Hepatitis B co-infection or TB co-infection. Measurement of CD4 cell count is the preferred method for ART eligibility assessment in HIV-positive patients. However, in sub-Saharan Africa, this is still not widely available[11]. It is important to note

Corresponding Author: ACP/DR. Samuel Otu-Nyarko**,** Police Hospital
P.O.Box: PMB CT 104, Accra
Tel: +233244060395
E-mail: otunyarkos@yahoo.com
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that CD4 cell count criterion is superior to clinical staging[12]. Many health settings in Africa do not have the resources to test for CD4 cell counts and plasma viral load and in these areas, a patient's HIV stage is assessed on the basis of clinical criteria alone, using the WHO HIV clinical staging. Those at WHO stage 3 or 4 can be eligible for ART[13, 14]

With insufficient resources to test CD4 cell counts and plasma HIV viral load in many resource-limited settings, including many of the regions hardest hit by the HIV/AIDS epidemic, clinicians must rely on clinical parameters when assessing a patient's disease status[15]. In Ghana, though the National Guidelines encourage the use of CD4 cell counts, frequent breakdowns of the machines and stock out of reagents means WHO clinical staging guidelines are used to decide whether to initiate treatment on ART or not. Patients with low CD4 counts that are staged WHO 1 or 2 could be denied treatment with ARV medication for long periods till the CD4 cell count results are available.

Although the WHO clinical staging system has been widely adopted as a tool for assessing ART eligibility, healthcare workers find it time-consuming, complex and poorly applicable in resource-poor settings without access to sophisticated diagnostics[16]. When used for individual treatment decisions, WHO clinical staging misses a high proportion of individuals who are ART eligible by CD4 cell count. Access to accurate, accessible, robust and affordable CD4 cell count testing methods will be a pressing need for as long as ART initiation decisions are based on criteria other than seropositivity[7].

Objective

To determine whether WHO clinical staging is predictive of CD4 of 350 in initiation of ART in patients presenting at the Police Hospital ART clinic.

Methods

Study site

This study was conducted at the Police Hospital in Cantonments, Accra. It was established initially to take care of the health care needs of only Police Personnel and their dependents in 1976. However, this has changed and currently, over 80% of out-patient attendants are civilians.

It is located in an urban area, which is Cantonments, in the La Dade Kotopon Municipal area. Care for PLHIV started in 1995, with the use of food supplements and psychological support. In 2007, a team comprising Medical Doctors, Nurses and Pharmacists were trained by the National AIDS Control Programme (NACP) to start treatment with ARV medication. Actual treatment started in the first quarter of 2008.

Study design

This was a cross-sectional study, with review of secondary data retrieved from the records of HIV infected patients. We reviewed data over a three year period, from January 2010 to December 2012.

Selection criteria

Initially 350 records were retrieved for the period. We excluded persons below age 15, patients infected with hepatitis B and pregnant women. Two hundred and five records met our inclusion criteria.

Data capture and analysis

Data entry sheets were used to capture the required information from the folders of patients. It was entered into SPSS version 17 and analyzed with the same software. Records were anonimized with the use of codes and stored securely in a lockable metallic cabinet. We looked at the initial WHO clinical classification of the client and compared it to the initial CD4 count results.

Results

The total number of patients selected for the study was 205. As shown in table 1, the minimum age was 15 with the maximum being 71years. The mean age was 36.7 years.

Table 1: Age Groups of Patients

Age Group	Number of Patients
15 - 19	2
20 – 24	13
25 – 29	46
30 – 34	38
35 – 39	29
40 – 44	25
45 – 49	24
50 - 54	10
55 - 59	11
60 - 64	3
65 - 69	2
70 - 74	1

The majority 142 (69.3%) were females. Eighty seven percent were Christians (178), with 9.8% Muslims (20), whilst the rest did not have any religion indicated.
The educational level of clients is shown in table 2.

Table 2: Highest Educational Level Attained by Clients

Educational Level	Number	Percentage
Tertiary	29	14.0%
Secondary	131	63.9%
Primary	18	8.8%
Nil	20	9.8%
Missing values	7	3.4%
Total	205	100%

Most of the patients (63.9%) had up to secondary level education, 14% had tertiary level whilst 8.8% had primary education. However, 9.8% had no formal

education. Almost 84% were infected with type 1 HIV, six persons (2.9%) had a mixed infection with both types 1 and 2, with one person having type 2 HIV only as depicted in table 3.

Table 3: Types of Hiv of Patients

HIV Type	Number	Percentage
1	171	83.4%
2	1	0.48%
1&2	6	2.9%
Missing value	27	10.8%
Total	205	100%

The lowest CD4 count value was 1, with the highest being 1517. The mean CD4 cell count value was 341. As in table 4, seventy percent of clients were in stage 1 or 2, whilst 30% were in stage 3 or 4 according to the WHO clinical classification.

Table 4: Who Clinical Stages of Clients

Who Stage	Number	Percentage
Stage 1	127	62.0%
Stage 2	16	7.8%
Stage 3	57	27.8%
Stage 4	5	2.4%
Total	205	100%

Sensitivity of the WHO Clinical Staging in predicting CD4 for initiating ART was low (44%) and specificity quite high (87%). Positive predictive power was 83% and Negative predictive power was 51%.

Limitations:
This study was done in a single urban ART clinic in Accra, thus the findings may not be generalized on the entire population of Ghana.

Discussions

Certain groups of patients could have little or no clinical manifestations but have very low CD4 counts (<350), indicating a very weak immune system. Using the WHO classification alone, the treatment for this group of patients will be delayed to their detriment. Such patients could therefore be staged WHO 1 & 2 and with the absence of CD4 count results, their treatment with ART will be unduly delayed. In most countries in sub-Saharan Africa, there are more females than males infected with HIV. This trend was apparent in our sample where 69.3% were females. A similar figure of 68% was found in other studies[17]. We found a mean age of 36.7 years which again was comparable to findings in other studies[17].

Seventy percent of our patients were classified as WHO 1 or 2, whilst 30% were classified as 3 or 4. Approximately the same figure was also found in Kenya[18] but these figures differ from a study in Uganda[17], where 61% were staged 1 or 2. In our study, 48.9% of those needing ARV treatment as per CD4 count were classified as WHO stage 1 or 2. This means that 48.9% or almost half of those deemed not qualified to start ARV actually needed to start on ARV. This is in agreement with a figure of 48% found in a study in Uganda[19]. Many patients who needed treatment were therefore not considered for treatment on the basis of CD4 clinical staging. Again we found that 17.2% of those that were started on treatment were not to have started on treatment based on WHO clinical staging. They were staged 3 and 4 but had CD4 cell count above 350. This was however not to their detriment as the sooner the treatment is started, the better. Our figure of 17.2% was however higher than that found in Uganda19 which was 12%.

In a similar study among women in Kenya20, out of a total of 2,915 that met the CD4 cell count criteria for starting ARV medication, only 23% had WHO stage 3 or 4. Meaning 73% would have missed out on ARV treatment using the WHO clinical staging alone. This figure is higher than what we found. Also among women who were staged 1 or 2 using the WHO clinical classification, 42% actually had to be put on treatment as per CD4 cell count results[20]. This is lower than what we found which was 48.9%. Our finding compares favourably with almost 50% found in Uganda[17].

Sensitivity was low in our study (44%), the same of which was found in other studies[17,21]. However a higher figure of 63% was found in Kenya[18]. We found specificity of 87% almost the same as 85% in other studies[21].

Conclusion

We found that almost 50% of those staged WHO 1 or 2 actually needed to be put on ART as compared to their CD4 cell counts. The start of their treatment could have been unduly delayed to their detriment. The WHO clinical staging misses a high proportion of patients that are qualified to initiate ART using CD4 of ≤ 350 as a cut – off point. when used alone without CD4 count.

Recommendation

The National AIDS control programme should ensure that there are enough CD4 machines in health facilities. Stock outs of reagents should be avoided since this also compounds the delay even when the CD4 machines are available. The programme must aim at basing the commencement of treatment solely on CD4 cell count results in the future.

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