

Association of CD4 T cell Recovery and Interpersonal Trust in Patient-Physician Relationship among HIV-Infected Adults in Hospital for Tropical Diseases, Vietnam

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ABSTRACT

The global HIV/AIDS pandemic is still dangerous due to high incidence and high mortality rate. There are many factors associated with the immunological response beside treatment with medical practice. This paper aimed to assess the correlation of immunological responses and trust in physician measures in adult patients living with HIV/AIDS. A cross-sectional was studied to find the association between CD4 T cell changes and interpersonal trust in patient-physician relationships. This study was carried out 93 adult patients (male accounted for 83.9%) who were newly diagnosed with HIV/AIDS infection at outpatient clinics, Tropical Diseases Hospital from October 2018 to August 2019. The mean TCD4 increased by 324.7 cells/ μ l and 379.7 cells/ μ l, respectively, compared to the original of 161.7 cells/ μ l. Almost all patients had their immunity recovered after 3 and 6 months and the majority of patients have achieved virological success after 6 months of treatment. Factors associated with early immune recovery are: youth, lower-secondary education and single status. The majority of patients had truly trust in physician after 1 month and factors associated with trust in physician scale are: male and employed. In Spearman rank correlation, CD4 T cell recovery and the trust present a strong relationship with $p=0.008$. Our finding is that the initial immunity recovery was strongly influenced by the interpersonal trust between the patients and the healthcare workers.

KEYWORDS: HIV/AIDS, ART, TCD4, TPS

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ABBREVIATIONS:

HIV/AIDS: Human immunodeficiency virus / Acquired immunodeficiency syndrome

ART: Antiretroviral therapy

TCD4: Lympho T cluster of differentiation

BMI: Body mass index

TPS: Trust in physician scale

I. INTRODUCTION

The global HIV/AIDS pandemic is still dangerous with high incidence and high mortality rate [1]. No cure and vaccine have found for this disease until now. The major hope for HIV infected patients is to prolong their lives with the ART which has been shown to be effective in improving the quantity of CD4 T cells [2]. However, there are many factors associated with the immunological response besides treatment with medical practice. The amount of control exerted by clinicians and patients in medical interactions has long been viewed as a critical aspect of health care. While some studies have shown that TCD4 recovery is associated with adherence [3] and psychological stress of patients [4,5], others have not noticed a significant association between immunity recovery and interpersonal trust in patient-physician relationships. In chronic disease management, concern and desire of patients now turned into priority in medical interactions. One important construct in patient-clinician relationships that may be related to patient's

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desires for control is interpersonal trust [6]. This study aimed to assess the correlation of immunological responses and trust in physician measures in adult patients living with HIV/AIDS in Ho Chi Minh city, VietNam.

II. MATERIALS AND METHODS

Study design: This was a clinic based longitudinal study done at outpatient clinic, Tropical Diseases Hospital from October 2018 to August 2019.

Study setting: The study was conducted at outpatient clinic, Tropical Diseases Hospital, Ho Chi Minh city, VietNam. Tropical Diseases Hospital is a researching and teaching hospital for medical students in Mekong River Delta - southern VietNam. The hospital runs both inpatient and outpatient treatment activities, with an approximate bed capacity of 500. Providing treatment and taking care of HIV patients is one of the core parts of outpatient activities. This unit serves more than a thousand patients per year.

Study participants: The study involved 93 adult HIV-infected patients aged 18 and above who enrolled in HIV care and initiated on first line ART, with a minimum follow up of 6 months.

Data collection and laboratory analysis: The adult HIV patients on first line ART with a minimum follow up of 6 months were invited to participate in this study. These patients are usually followed up monthly or after every 3 months depending on their clinical status. TCD4 measurements are usually routinely performed after every 3 months. After giving consent, a structured questionnaire was used to collect information regarding, epidemic data, date of diagnosis of HIV, date of ART initiation and regime, compliance level which was assessed using patient response method, trust in physician score, BMI, comorbidities, co-medication, TCD4 and others routine laboratory.

Assessment of interpersonal trust in patient-physician relationships: Interpersonal trust in patient - physician relationships was measured by using the TPS (developed by Anderson & Dedrick with 11 - item scale [6]). Findings from many studies are reported and supplied further evidence of the reliability and validity of the scale of the Trust in Physician scale. With Cronbach' alpha from 0.85 to 0.90. Trust was significantly related to patients desires for control in their clinical interactions and subsequent satisfaction with care [6-9].

Statistical analysis: The data was entered, verified and cleaned, using Epidata spread and the data analysis was done using STATA. Continuous variables were summarized by medians and interquartile ranges, and categorical variables were summarized by frequency and percentage.

Definitions of early immune responses: Immunologic response (CD4 T cell increase) after 3 months of treatment more than 50 cells/ μ l is defined as an early immune response [10].

Consent to participate:

The consent to participate in the study was taken from all study participants because the study only recorded patients who provided written consent. All patients with immunological failure were switched into second line of ART following failure of improvement of their TCD4 two weeks of intensified adherence and in some with virological proof of ART treatment failure as per existing treatment guidelines. Patients who declined consent were not denied their services (study was approved by the Human Research Ethics Committee of the Hospital for Tropical diseases in Ho Chi Minh city, dated 18-10-2018).

III. RESULTS

Between October 2018 and August 2019, 93 people provided informed consent to participate in this study. Almost all patients were male (83.9%). The median age was 30 (IQR 26-39). Majority of participants were employed (73.1%) and married (55.9%). Most of the study participants (94.6%) had attended primary school and above.

An analysis of the six-month increase in CD4 cell count demonstrated that, the slope of the plotted overall CD4 cell count increased significantly ($p<0.05$ compared with the previous six months) and the steepest increase in the first 3 months, that shows in **Table 1**. The proportions of patients who achieved CD4 cell counts of ≥ 200 cells/ μ l (AIDS-related, based on the WHO criteria for immunological stage) after receiving 3 and 6 months of suppressive ART were 55% and 73%, respectively.

Table 1 Baseline recovery TCD4 (n=93)

Variable	0 month	3 months	6 months	p value
Recovery TCD4 cell				
Median baseline TCD4 (cells/ μ l) *	161.7	324.7	379.7	p1< 0.001 p2< 0.001 p3< 0.001
AIDS-related in group with low TCD4 (<200 cells/ μ l)				
Percent patient recovery	0%	55%	73%	

*Wilcoxon signed-rank test

p1, p2: at point 3 months and 6 months compared to the original; p3: at 6 months compared to 3 months

The changes in CD4 lymphocyte count the study on the third month were significantly associated with a degree of age (immunity recovery was more popular among younger patients than the older) (**Table 2**). On the sixth month, early immune recovery was significantly associated with marital status (single) and education level (below secondary) (**Table 3**).

Table2. Factor association with early immune responses at 3 months

Characteristics	Percent patient had early immune responses %/ (n)	p value	PR (CI 95%)
Age	-	p= 0.04	r= - 0.2*
Gender			
<i>Male</i>	87.2 (68)		-
<i>Female</i>	66.7 (10)	0.15	0.76 (0.52 – 1.0)
Educational level			
<i>Primary</i>	80.0 (4)		-
<i>Secondary</i>	100.0 (34)	0.19	1.31 (0.87 – 1.96)
<i>Tertiary and above</i>	84.1 (40)	0.82	1.05 (0.69 – 1.59)
Marital status			
<i>Single</i>	84.2 (34)		-
<i>Married</i>	80.0 (44)	0.7	0.95 (0.72 – 1.23)

Occupational status			
<i>Have employed</i>	83.8 (57)		-
<i>Unemployed</i>	85.7 (21)	0.89	1.02 (0.73-1.42)
BMI			
< 18.5	79.2 (19)		-
≥18.5	83.9 (47)	0.63	1.06 (0.83-1.34)

* Spearman's rank correlation coefficient

Table3. Factor association with early immune responses at 6 months

Characteristics	Percent patient had early immune responses %/ (n)	p value	PR (CI 95%)
Age	-	p= 0.1	r= - 0.1*
Gender			
<i>Male</i>	96.1 (75)	-	-
<i>Female</i>	93.3 (14)	0.69	0.97 (0.84 – 1.12)
Educational level			
<i>Primary</i>	100.0 (5)	-	-
<i>Secondary</i>	90.5 (19)	0.02	0.86 (0.76 – 0.97)
<i>Tertiary and above</i>	97.7 (46)	0.001	0.93 (0.89 – 0.97)
Marital status			
<i>Single</i>	100.0 (40)	-	-
<i>Married</i>	93.8 (30)	0.002	0.89 (0.83 – 0.96)
Occupational status			
<i>Have employed</i>	97.1 (66)	-	-
<i>Unemployed</i>	14.3 (2)	0.66	0.88 (0.65-1.20)
BMI			
< 18.5	91.7 (22)	-	-
≥18.5	92.3 (55)	0.29	1.00 (0.82-1.23)

* Spearman's rank correlation coefficient

The six-month changes in the median TPS scores after the commencement of treatment were plotted in **Table 4**. The majority of participants had high scores in TPS after 1 month in process, and it continued to increase significantly after 3 and 6 months, with p<0.001.

Table4. Score of Trust in Physician scale

Variable	1 month	3 months	6 months	p value
Median of TPS score (IQR)	93.18 (88.64 – 97.72)	97.73 (93.18 – 100)	100 (97.73 – 100)	p1< 0.001 p2< 0.001 p3< 0.001

* Wilcoxon signed-rank test

p1, p2: at point 3 months and 6 months compared at 1 month; p3: at 6 months compared to 3 months

In study, after 6 months, the result showed that higher TPS scores were likely to appear in patients who were employed (p=0.04) and in male patients (p=0.01). Meanwhile, TPS is the most strongly associated with a patient's immunity recovery, with p=0.008.

Table5. Factor association with Trust in Physician scale

Characteristics	TPS at 3 months (Median)	Test, p	TPS at 6 months (Median)	Test, p
Age	-	r=-0.06 ³ p=0.5	-	r=-0.1 ³ p=0.1
Gender				
<i>Male</i>	97.73	Z=1.1	100	Z=2.5
<i>Female</i>	95.45	0.21	97.73	0.01 ¹
Educational level				
<i>Primary, Secondary</i>	97.73	χ ² =3.1	100	χ ² =6.1
<i>Tertiary and above</i>	97.73	0.52 ²	100	0.1 ²
Marital status				
<i>Single</i>	96.59	χ ² =2.0	100	χ ² =2.3
<i>Married</i>	95.45	0.52 ²	100	0.5 ²
Occupational status				
<i>Have employed</i>	95.45	χ ² =1,0	100	χ ² =6,1
<i>Unemployed</i>	96.59	0.6 ²	98.87	0.04 ²

Have religious beliefs				
Yes	97.73	$\chi^2=8.6$ 0.06 ²	98.87	$\chi^2=1.9$ 0.5 ²
No	97.73		100	
BMI		$\chi^2=0.9$ 0.6 ²		$\chi^2=4.1$ 0.1 ²
<18.5	95.45		100	
≥ 18.5	97.73		100	
Immune responses (TCD4 recovery)	r= 0.1 p= 0.3 ³		r= 0.3 p= 0.008 ³	

¹ Wilcoxon signed-rank test; ² Kruskal-Wallis rank test;

³ Spearman's rank correlation co-efficient

IV. DISCUSSION

This retrospective study was carried out to assess the trends in CD4 cell recovery among HIV patients after initiation of ART and the effect of baseline characteristics on CD4 cell count response. After the start of suppressive ART in an immune suppressed HIV-infected person, the rise in CD4+ T-cell counts characteristically exhibits a biphasic pattern. A steep initial phase likely reflects redistribution of cells from lymphoid tissue over the first few months of treatment as suppression of viral replication reduces immune activation [11]. Improvements in overall CD4 cell count among the patients were seen over time after 6 months. These findings are consistent with the retrospective longitudinal study conducted in Uganda in which the median CD4 lymphocyte count was found improving over time [12]. Other study in U.S showed that the median CD4 cell count continued to rise even up to 10 years after ART initiation, with the steepest increase in the first 3 months [13]. Similarly, many studies also clearly investigated that CD4 cell counts increased significantly after 6 months of the initiation of ART [12, 14, 15, 16].

These results suggest that analyses should examine CD4 cell count changes after 12 weeks from the initiation [14]. Analyses that separate the initial phase of CD4 cell count increase may be needed because different factors seem to influence this steep phase.

In the present study, the factors that pose a positive effect on CD4 recovery rate include: younger baseline age, single status, and low education level (secondary and below). Younger patients appeared capable of rebuilding their immune systems faster than those aged older. Previous studies have often categorized age to distinguish older patients, where older age usually resulted in slower recovery [12, 13, 15, 16, 17]. This can be explained by decreasing thymic volume with increasing age. Whereas, some other factors associated with immunological response included single status, and education level (secondary and below) may belong to characteristics and adherence of patients.

The results of this study give the information about that most participants had high scores in TPS after 1 month in process, and it continued to increase significantly after 3 months and after 6 months. With respect to the faith findings, TPS scores were found to be associated with male patients who were employed. Given that TPS are the most strongly associated with a patient's immunity recovery, the possible explanation for this is due to psychosocial of patients.

Doctor-patient communication is a major component of the process of health care. "The patient will never care how much you know, until they know how much you care." (Terry Canale

- American Academy of Orthopaedic Surgeons Vice Presidential Address) [18]. Effective doctor-patient communication can be a source of motivation, incentive, reassurance, and support. Several studies have demonstrated that psychosocial factors predict faster disease progression in HIV [5, 19, 20]. One of the major hypotheses of behavioral medicine is that stress hormones (cortisol, norepinephrine) may provide a link between psychological stress and health outcomes. When a new medication is started, a brief measure of perceived stress will be used rather than a more extensive measure of life events. Additionally, good doctor-patient communication has the potential to help regulate patients' emotions, facilitate comprehension of medical information, and allow for better identification of patients' needs, perceptions, and expectations. On the other hand, researchers often use patient satisfaction and adherence to determine the efficacy of the doctor-patient relationships. Improved doctor-patient communication tends to increase patient involvement and adherence to recommended therapy. At the same time, that leads to positive influence on patient satisfaction and healthcare utilization, and also improves outcomes of the treatment. Similar findings have also been reported by other authors that greater immunity recovery was associated with psychological status of patients [19- 23]. However, in order to increase credibility of the conclusion, further studies are recommended. Though not completely likely, some studies which were conducted from Ethiopia [24] and Tanzania [25] supported our result that adherence in ART is associated with immunity recovery.

As any other sample-based study, our analysis has limitations. This study was based on a single clinic, the results may not necessarily be generalizable. We examined changes only within a 6-month period to look for correlations of immunity status and mentioned factors. It is possible that CD4 changes over longer periods, which corresponds to more relevant factors.

V. CONCLUSION

To conclude, the majority of patients respond to first-line ART immunologically and trust in physicians. Early immune recovery is more common among younger patients than the older and factors associated with the immunity responses include: marital status (single) and education level (secondary and below). TPS scores were significantly associated with male patients who were employed. Our finding is that the initial immunity recovery was strongly influenced by the interpersonal trust in patient physician relationships. "Medicine is an art whose magic and creative ability have long been recognized as residing in the interpersonal aspects of patient-physician relationship" (Hall J. A - Communication of affect between patient and physician). The findings of this study add to the growing number of

factors that might be considered clinically important in maximizing the effectiveness of a new antiretroviral medication regimen.

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CONFLICT OF INTEREST

The authors declare no conflict of interest in this research.

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