



The trends of HIV late presenters in Sihanouk Hospital Center of HOPE and association between socio-demographic characteristics and late presentation to care service in Cambodia, 2003 - 2017

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Received February 20, 2021; revised March 30, 2021; accepted April 21, 2021

ABSTRACT

Introduction

In Cambodia, HIV treatment and care have become over burden on the current public health system. Despite the ART availability, patients continued to die and hospitalize, mostly because of their HIV advanced stages or late presentation to appropriate care services. We aimed to describe the trends of late presentation at care service of patients over time from 2003 to 2017 in Sihanouk Hospital Center of HOPE (SHCH), and to determine the association of socio-demographic characteristics with this late presentation.

Methods

We used data from SHCH electronic database by selecting all new HIV patients from March 2003 to December 2017 who were ART naïve with age ≥ 18 years old. In total, 5369 records were retrieved for analysis in Stata version 13. We calculated proportion of HIV late presenter from 2003-2017 using chi-square test for trends to detect significant changes. Bivariate analysis was used to determine association between socio-demographic factors and HIV late presenters, defined as CD4 count < 200 cell/ mm³.

Results

Of 5369 patients, the mean age at enrollment were between 35 (SD= 8.6) and 37 years old (SD= 10.2) over time from 2003-2017. HIV late presenters were slightly decreased from 66% (2003- 2007), 58% (2008- 2012), to 57% (2013- 2017) with p value < 0.001 . Males, age group > 30 years old, single/divorce, occupation, residence, and WHO stage 3/4 were most significantly associated with HIV late presentation to care service (p value < 0.05).

Conclusions

In spite of the national ART universal coverage policy with Test and Treat approach, HIV late presentation remained relatively high. Being males, older age, single/divorced, small businessmen, and people from Great lake region were identified as associated factors for late presentation. More effort needs to be invested for these populations to improve counseling, testing and linkage system to early ART care to prevent severe OIs and death.

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Citation: Srey P, Chan S, Choun K, Sopheab H. The trends of HIV late presenters in Sihanouk Hospital Center of HOPE and association between socio-demographic characteristics and late presentation to care service in Cambodia, 2003 – 2017, *CJPH (2021) 02:06*

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"Keywords: HIV late presentation; ART; Care service; Associated factors; Cambodia;"

Introduction

HIV epidemic has been known as a major public health concern globally [1]. There are an estimated 36.9 million individuals living with the HIV at the global level, and 5.2 million living in Asia [2]. Late HIV diagnoses and acute opportunistic infections (OIs) at first visit to care remained common [3]. After stabilizing their health, patients may challenge other complicated problems at the beginning of antiretroviral treatment (ART) such as immune reconstitution syndrome (IRIS), and adverse drug reactions. Consequently, most of patients were often ill, less responsive to ART and even have a high early mortality risk [4-7].

Late presentation had a major effect on healthcare utilization and expenditure because they spent high cost during the first few months for treatment and care [8]. Direct medical care costs were 200% higher for late presenters in Canadian patients [8, 9]. A study in Italy indicated that around 40% of HIV infected patients diagnosed at late stage of infection [10], while multicenter study in Asia found that 72% [4]. In Cambodia, late presenters decreased from 67% in 2003 to 41% in 2013 with CD4 count < 100 cells/mm³ [11]. The research from TREAT Asia found 72% were HIV late presenters [4]. In Sub-Saharan Africa, PLHIV late presentation to care services ranged from 29% to 42% [12].

Older age and males were commonly associated with late presentation due to health care providers were less likely to propose HIV testing [11]. The study in TREAT Asia in Shanghai, Singapore, and India found that older age and males were significantly risk factors for late presentation into care [4, 13-15]. Additionally, other associated factors were included migration, and injecting drug users (IDU) [16, 17]. They increased risks of HIV related death between 6-13 folds in Eastern Europe and Southern Europe [18]. It should be noticed that eligible criteria for ART initiation varied from countries to countries and over time in the past decade depending on the ART availability, selection of less toxic ART regimen, clinical practice and scale-up treatment program. First, it was recommended the threshold at CD4 count \leq 200 cells/mm³ in 2003 to 2007, then it was raised to \leq 250 cells/mm³ in 2007 to 2010; then to \leq 350 cells/mm³ in 2010 to 2017, and finally regardless CD4 count since 2017 [19-21].

In Cambodia with the universal access of ART, the trends of late presentation are still uncertainly reported since the initiation of Test and Treat approach. As a result, it could lead to underestimation not only the resources but also the ART management which is not properly covered to all populations. Therefore, this study aimed to describe the trends of late presentation at care service of the HIV patients over time from 2003 to 2017, and to identify risk factors associated with this late presentation.

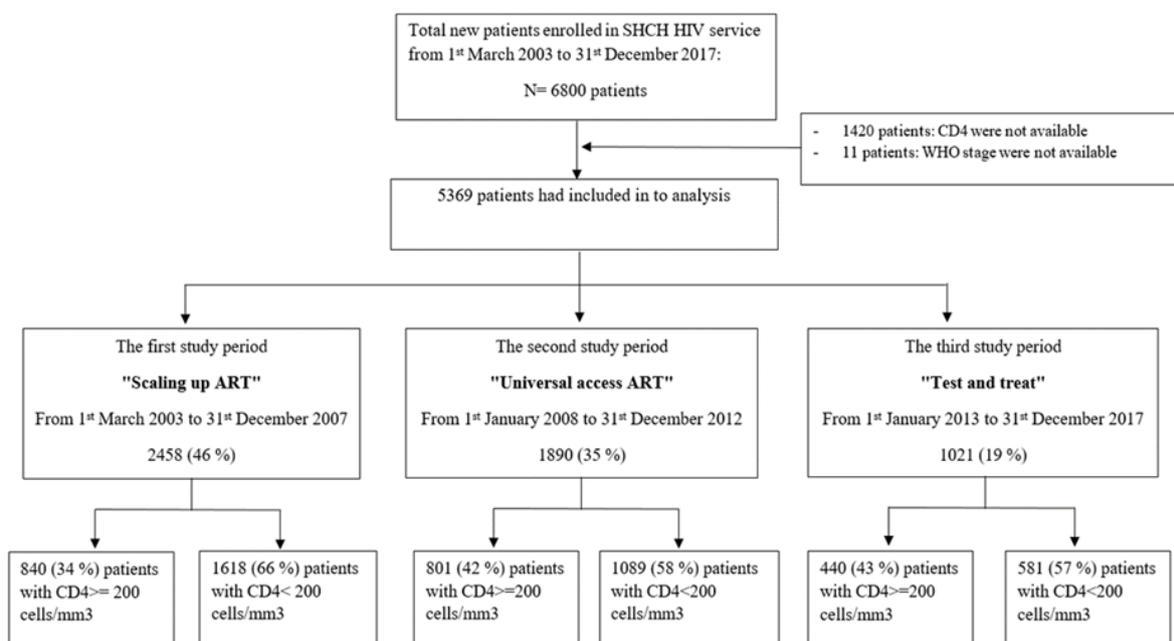
Methods

Data source and management

We used the routinely collected HIV data from SHCH electronic database in Microsoft Access. We retrieved the data with criteria indicating that all HIV patients had to be ART naïve, adults with age at least 18 years old enrolling in HIV care at SHCH between 1st March 2003 to 31st December 2017. Then, we imported it into Stata 13. In total, 6,800 patients were met the defined inclusion criteria. After further checking and cleaning, only 5,369 PLHIV were eligible and kept for analysis (**Figure 1**).

Data analysis

Analyses were performed in Stata V13. Basic characteristics of all ARV naïve patients including socio-demographic variables (age, sex, and occupation), immunological status (CD4 count), opportunistic infections, and clinical stages. They were described using frequency, proportion, mean (SD) and median. We calculated the proportion of HIV late presenter in the three periods: Scaling up ART (2003-2007), universal access (2008-2012) and test and treat period (2013-2017). We used chi-square statistics to test the significant changes overtime. Finally, the bivariate analysis was used to determine socio-demographic factors associated with HIV late presenters with statistically significant level at p value \leq 0.05. HIV late presenter or advanced HIV disease was defined as the presence of CD4 count < 200 cell/mm³ (WHO guideline 2017).

Figure 1: Eligible screening process for new HIV enrolled patients in SHCH between 2003-2017

Results

Socio-demographics characteristics of new HIV enrolled patients

Of 5,369 patients, female patients represented 52.3% (2003- 2007), 56.0% (2008-2012), and 49.0% (2013-2017). Most patients were in the age group of 31- 40 years old, and more than half of them were married. Also, most were manual labors with fewer housewives (**Table 1**).

The HIV late presenter at enrolment

Among 5,369 HIV naive patients, late presentations to care services declined slightly but significantly with 66% [95% CI: 63.9- 67.7] in 2003-2007, 58% [95% CI: 55.4- 59.8] in 2008-2012 and 57% [95% CI: 53.8- 59.9] in 2013-2017 with p value <0.001. Also, HIV patients presented in the hospital with advanced WHO clinical stage 3&4 were 70% in 2003-2007, 63% in 2008-2012 and 64% in 2013-2017 respectively with p value < 0.001.

Association between demographic characteristics and HIV late presentation

As shown in **Table 2**, men (74%) were likely presented to care services later than women (65%) overtime (p value <0.001). More than 60% of patients had CD4 <200 cells/mm3 in the age group more than 30 years old (p value <0.001). About 76% of

participants who had CD4 <200 cells/mm3 were single. Close to 76.0% (2003-2007) and 64.4% (2008-2012) of patients whose were small-businessmen more likely to come late in accessing care service than other groups. At least 70% - 76% of patients who were from the Great lake region had been found late presentation to HIV care overtime. Furthermore, over the study period between 2003-2017, about 75%-80% of patients with advanced clinical stage (stage 3 & 4) commonly presented late to clinical care with statistically significant level at p value <0.001.

Discussion

Overall, this study indicated the HIV late presentation to clinical care services remained relatively high in Cambodia over the past 15 years though high ART universal coverage with test and treat policy have been in place since 2013. Factors associated with late presenter included males, older age group over 30 years old, non-marrieds (single, divorced), group of people who run smaller business and PLHIV with advanced clinical stages.

Globally, HIV late presentation to care and treatment service was always a main concern for the public health system despite the availability of universal coverage of ART with the test and treat all approach.

Table 1: Socio-demographic characteristics of new HIV enrolled patients

Variable	2003- 2007		2008- 2012		2013-2017	
	N= 2458	%	N= 1890	%	N= 1021	%
Sex						
Female	1286	52.3	1056	56.0	498	49.0
Male	1172	47.7	834	44.0	523	51.0
Mean age (SD), in years	35 (8.6)		36 (9.2)		37 (10.2)	
Age groups in years	N= 2456	%	N= 1885	%	N= 1016	%
18- 30	800	32.6	636	33.7	284	28.0
31- 40	1095	44.5	740	39.3	429	42.0
41- 50	417	17.0	368	19.5	200	20.0
51- Max	144	5.9	141	7.5	103	10.0
Marital status	N= 2424	%	N= 1890	%	N= 1012	%
Married	1471	61.0	1194	63.0	546	54.0
Divorced	730	30.0	547	29.0	277	27.0
Single	223	9.0	149	8.0	189	19.0
Occupation	N= 2398	%	N= 1874	%	N= 1003	%
Skilled workers ⁽¹⁾	497	20.7	482	25.7	175	17.4
Manual labors ⁽²⁾	1130	47.1	862	46.0	388	38.7
Small business	453	18.9	382	20.4	291	29.0
Housewives	0	0	0	0	14	1.4
Entertainment workers ⁽³⁾	5	0.2	2	0.1	7	0.7
Others ⁽⁴⁾	313	13.1	146	7.8	128	12.8
Residence	N= 2451	%	N= 1888	%	N= 1018	%
PNP and coastal region ⁽⁵⁾	405	16.5	203	10.8	82	8.0
Plain region ⁽⁶⁾	119	4.9	67	3.5	29	2.9
Great lake region ⁽⁷⁾	104	4.2	51	2.7	27	2.7
Plateau/Mountain region ⁽⁸⁾	1823	74.4	1567	83.0	880	86.4

(1) Skilled worker: Manager, NGO, Company staff, Librarian, Medical staff, Military/Police/Soldier, Teacher. (2) Manual labors: Cleaner, Farmer, Fisherman, Garbage collector, Garment worker, Hair dresser, Nail worker, Laborer, Security, Taxi/Moto/Cyclo driver, Migrant. (3) Entertainment workers (EW), FSW. (4) Other: Jobless, Monk, Retired, Student, Others. (5) PNP and coastal region: Phnom Penh, Kampot, Koh Kong, Kep, Kampong Som. (6) Plain region: Kampong Cham, Tbong Khmum, Kandal, Prey Veng, Svay Rieng, Takeo. (7) Great lake region: Banteay Meanchey, Battambang, Pursat, Kampong Chhnang, Siem Reap, Kampong Thom. (8) Plateau, mountain region: Kratie, Stung Treng, Preah Vihear, Monduliri, Ratanakiri, Kampong Speu, Pailin, Ordor Meanchey.

The current study indicates that late presenters are relatively high over the past 15 years that was consistent with the context in most developing countries. From the global literature, prevalence of late presentation to ART service varied from country to country, from developing to developed countries. For example, In Asia, the prevalence of late presentation ranged from 45% (China), 74% in Asia Pacific region, to 83% in India [4, 14, 15, 22]. On the contrary, the prevalence of HIV late presenters was relatively lower in Europe and the USA and most developed countries. The low HIV late presentation in these developed countries were possibly due to the early and more widespread testing by provider's initiative testing policies, timely referrals after positive test results and, massive scale-up of antenatal screening for HIV [18, 23].

In this study the prevalence of late presentation was still higher than most developed countries but comparable to many developing countries. This may be due to limited availability of one stop service.

Some Voluntary Confidential Counseling and Testing (VCCT) and OI/ART clinics often haven't shared the same location. For instance, VCCTs are standalone at local health centers, while OIs/ART services are located at referral hospital or national hospitals. Office's working hour's is not widely opened regularly in morning and afternoon at OIs/ART clinics. HIV testing is less likely to be proposed by health care providers to individuals as they are assumed to be lower risk. Despite the comprehensive care at SHCH OIs/ART clinic with 24-hour care for in-patients and 8 hours per day from Monday to Friday for out-patients consultation, the patients with late presentation to HIV care services, might be due to their limited HIV care knowledge, awareness about the service, unknown their HIV status due to delayed testing, and seeking appropriate care service. Consequently, once they were able to access care at SHCH, they were severely sick with advanced stage and already late though the service was responsive enough.

Table 2: Association between socio-demographic characteristics and HIV late presentation at enrollment

Variable	2003- 2007			2008-2012			2013-2017		
	Late presenter*	%	P-value	Late presenter	%	P-value	Late presenter	%	P-value
Sex	N= 2458			N= 1890			N= 1021		
Female	752	58.5	<0.001	544	51.5	<0.001	277	55.6	0.419
Male	866	73.9		545	65.4		304	58.1	
Age groups (years)	N= 2456			N= 1885			N=1016		
18- 30	477	59.6	<0.001	266	41.8	<0.001	112	39.4	<0.001
31- 40	757	69.1		480	64.9		266	62.0	
41- 50	286	68.6		248	67.4		133	66.5	
51- Max	96	66.7		92	65.3		68	66.0	
Marital status	N= 2424			N= 1890			N= 1012		
Married	927	63.0	<0.001	651	54.5	<0.001	311	57.0	<0.001
Divorced	502	68.8		360	65.8		185	66.8	
Single	169	75.8		78	52.4		79	41.8	
Occupation**	N= 2393			N= 1872			N= 982		
Skilled workers	333	67.0	<0.001	291	60.4	<0.001	85	48.6	0.071
Manual labors	672	59.5		450	52.2		226	58.3	
Small business	343	75.7		246	64.4		164	56.4	
Others	225	71.9		94	64.4		82	64.1	
Residence	N= 2451			N= 1888			N= 1018		
PNP and coastal region	270	66.7	0.139	139	68.5	<0.001	57	69.5	0.032
Plain region	78	65.6		32	47.8		18	62.1	
Great lake region	79	75.9		36	70.6		19	70.4	
Plateau, mountainous	1184	64.9		880	56.2		485	55.1	
WHO stage	N= 2458			N= 1890			N= 1021		
1 or 2	237	32.4	<0.001	198	28.2	<0.001	85	23.2	<0.001
3 or 4	1,381	80.0		891	75.0		496	75.7	
BMI***	N= 2279			N= 1876			N= 1007		
Underweight	169	69.3	0.009	112	57.4	0.956	52	59.8	0.186
Normal weight	1,127	64.6		801	57.8		412	57.7	
Overweight & obesity	166	57.0		167	56.8		105	51.0	

*Late presenter: CD4 < 200 cells/mm³ ** Occupation: we excluded housewives and entertainment workers due to few numbers.

*** BMI: We combined overweight and obesity.

Factors associated with HIV late presentation to care service

Being male was associated with late presentation, and this result shared similarity with previous studies in Asia, and in Europe such as Netherlands and Italy [4, 13-17]. This may be due to male was less likely to use VCCT services as a part of routine care services compared to women particularly during their ANC checkup. Also, self- perception on health and illness and need health care access maybe lower among men than women [24, 25].

Older age was also associated with late presentation to the HIV care service. This was well reported in the past literature in Asia, Europe and Mexico [4, 13-16,

18, 26, 27]. Older patients were more likely to be diagnosed during hospitalization as HIV testing is less likely to be suggested by physicians to old patients, assuming the risk to be low.

Several variables related to marital status and occupation were associated with HIV stage at presentation. Being divorced or non-marrieds were associated with late presentation as compared with being married suggesting their low caring with worse health condition. In addition, the majority of HIV late presenters were mostly small businessmen in the period 2003- 2007 and 2008-2012 with p-value < 0.001. This may be due to health seeking behaviors of patients and lack of awareness of the risk of HIV

infection, or economically affordable to seek private care service until late to advanced clinical stage.

Overtime, the finding indicates that more than 70% of patients lived in Great lake region were late presentation to care. Their access to HIV care might be problematic due to the long distance from service, financial hardship, or limited access to local care service. Also, a high correlation between advanced clinical stages and late presentation may suggest their lateness of health care seeking behaviors, limited awareness of health care services, and poor awareness of the risk of HIV infection. Stigma and discrimination might also contribute to this late access to appropriate care service.

Our study had several limitations. First, as a hospital routine program data, it could not represent nationally. Secondly, behavioral risk exposure (i.e. MSM, IDU or risk groups) particularly clinical (OIs) data were not collected in this study due to the linkage issue with main data resulting in limited analysis to identify or compare OI between later presenters vs. non late presenter. Missing data are also common when using routine data. However, due to the small missing data (<1%) it should not affect our findings. Thirdly, it was also hard to identify for naïve patients if he/she used to enroll elsewhere and didn't report their medical history, but it was small proportion of patients who didn't disclose their medical history

Conclusion

In spite of the national ART universal access policy, and test and treat approach, HIV late presentation remained relatively high. Being male, older age, single/divorced, small businessmen, and people from Great lake region were identified as associated factors with HIV late presentation to care service. More effort needs be done for these specially population to improve HIV counselling, testing and linkage system for early ART care and to prevent severe OIs and death. Further study should be conducted with better linkage system with clinical data.

Acknowledgement

Authors would like to acknowledge and thank all patients, staff in Infectious Disease Department and the Management of Sihanouk Hospital Center of HOPE for making the data available for this study.

Ethical approval

The study had posed no risk to all participants. No patient identifiers were included in the datasheet for analysis as we used ID code instead of name. All patients included in the original SHCH database were given written inform consent for their clinical records to be used in this study. This study was approved by to Cambodia NECHR on 26th March 2019 (Ref. # 075).

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