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HIV impact on women: gender difference among late testers and advanced HIV infection

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Abstract. This study reported the effect of gender difference on HIV seropositive late testers or advanced infection. A retrospective cohort study of newly diagnosed HIV seropositive based on adatabase in the main referral hospital in Denpasar, Bali, Indonesia from 2004 – 2016. Women and man were categorized as late testers (CD4 ≤ 200 cells/uL and/or AIDS diagnosis ≤ 12 months from first HIV test date). Non-late testers (CD4 > 200 cells/uL and/or no AIDS diagnosis during study period or diagnosis of AIDS >12 months from HIV diagnosis), of reproductive age (13 – 49 years old), and not of reproductive age (>49 years old). Logistic regression was used to estimate risk and its statistical significance. The model consists of gender and age correctly classified 83.5% of cases. Women were almost two times more likely to present as non-late testers compared to men, and reproductive age of 15 – 49 years were 1.5 times more likely to present as non-late testers compared to those with age > 49 years. Women affected by HIV almost in equal as for men. Women and those within reproductive age were more likely to present before the advanced stage compared to men and those aged > 49 years.

1. Introduction

Since the global HIV epidemic begins, in many regions of the world women have remained at a higher risk of HIV infection than men. Globally, women living with HIV account for half of all adult living with HIV an estimated 17.8 million women aged 15 or older living with HIV around the world.[1,2] In United States, one in four Americans living with HIV is awoman.[3] In most of the world, as asociety still emits value judgment that assigns particular roles and relationship to women and men, being women poses a vulnerability to HIV infection.

Women were vulnerable to sexually transmitted diseases, HIV in particular, due to biological, epidemiological and social factors.[4,5] HIV requires live cells for transmission, and semen has higher cell content compared to vaginal fluid thus more infectious.[6] The semen remains in vaginal and rectal longer compared to vaginal fluid on the penis, therefore women will be exposed to HIV longer in cases with unprotected sexual contact. Vaginal mucous in adolescent and postmenopausal women is not as thick and mature to serve as a barrier, and more permeable to HIV infection. Some sexually transmitted infection in women were asymptomatic and go unnoticed, along with tearing and hemorrhaging during sexual relations also more common in women; either due to traumatic coitus, rape, microscopic fissures or menstruation, further adding to women vulnerability to HIV infection.[6,7]

Most Asia countries as elsewhere in the developing world, sex-based socioeconomic disparities play a significant role in the spread of HIV. Women lack control over their body, sexual and economic

life, women were held responsible for family planning and the use of contraceptive where the partner reluctant in using a condom. There was also the culture of limited communication on sexual topics, and most women thus assume their partner is faithful. Teen pregnancy also still common and also domestic violence, all contribute to social factors in women vulnerability to HIV infection.[8, 9]

As a result of these biological, epidemiology and social factors, women were accounted for 35 percent of adults with HIV in Asia at the end of 2013 up from 21percent in 1990.[10] The number even more striking globally where women represent 49 percent of all adults living with HIV and in endemic regions.The african and carabian women account for 60 percent of people living with HIV. Twenty years ago, the awareness aroused on gender inequality as a major burden for women to achieve equal opportunity in maintaining health and wellbeing. As UNAIDS has endorsed a commitment to ending the AIDS epidemic by reducing HIV infections to less than half a million per year by 2020 this means reducing new infections among women by at least 75 percent and achieving 90–90–90 treatment targets (90 percent of people living with HIV knowing their HIV status; 90 percent of people who know their HIV-positive status receiving treatment; and 90 percent of people on HIV treatment having a suppressed viral load). Women play crucial role in ending new infection by preventing vertical and horizontal transmission once their viral load undetectable and should have equal opportunity in accessing HIV care without the gender inequality burden.[7,8,9]

We realize that tackling gender inequality is a key in reducing women's vulnerability to HIV infection and ending the global AIDS epidemic, therefore we need the clear picture on the matter. To address that problem, we need to assess whether gender difference affects late testers and advanced HIV infection.

2. Methods

We enrolled a cohort of newly diagnosed HIV seropositive cases at the main referral hospital in Denpasar, Bali, Indonesia. The database obtained from 01 January 2004 until 31 December 2016. Diagnosis of HIV infection was made based on HIV 1 & 2 antibody test using three different methods. The CD4 baseline used in theanalysis was the CD4 level when initially diagnosed with HIV infection. Risk factors assessment for HIV transmission and demographic data extraction were done by using a local standard data form and obtained at baseline.

Advanced HIV infection defined as HIV seropositive men or women with AIDS-defining illness or WHO clinical stage 3 or 4, or CD4 less than 200 cells/uL. Men and women were categorized as late testers (AIDS diagnosis ≤ 12 months from first HIV test date), non-late testers (no AIDS diagnosis during study period or diagnosis of AIDS >12 months from HIV diagnosis), of adult reproductive age (15 – 49 years old), and not of reproductive age (>49 years old). Mann-Whitney U test was used to the median difference between groups. Logistic regression was used to calculate the likelihood of late testers.

3. Results

There were 6192 newly diagnosed HIV infection during thestudy period (Table 1) with increasing trend of new seropositive cases over the years (Figure 1). Woman to man ratio of 2: 3 was relatively constant over the years. This last decade, heterosexual activity contacts become the most common risk factor for HIV transmission. IVDU was the leading risk in theearly 2000s and less prominent in recent years. Male homosexual activity as HIV transmission's risk showed exponential growth with new case finding increase more than five times in the last five years and become the second most common risk for HIV transmission (Figure 2). The median CD 4 level at baseline was 59 cells/uL (range 1 – 1390 cells/uL).

Table 1. Baseline characteristics and clinical profile of 6192 newly diagnosed HIV infection in Denpasar's main referral hospital from 2004 – 2016.

	Values
Gender (female), N (%)	2334 (37.7)

Age (years), median (range)	31 (< 1 – 82)
Risk factors, N (%)	
- Multi-partner heterosexual	- 4926 (79.6)
- Multi-partner homosexual	- 660 (10.7)
- Multi-partner bisexual	- 82 (1.3)
- IVDU	- 442 (7.1)
- Perinatal	- 66 (1.1)
- Transfusion	- 1 (0.0)
- Other	- 15 (0.2)
CD4 (cells/uL), median (range)	93 (0 – 1390)

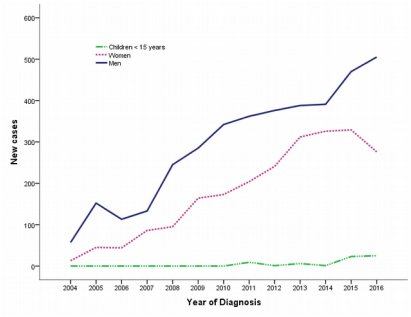

Figure 1. An annual number of new HIV infection between 2004 – 2016.

Among 6127 newly diagnosed HIV seropositive aged 15 years or older; 93.9 percent (5754/6127) were within thereproductive age range of 15 – 49 years. Four in every 5 newly diagnosed HIV seropositive in reproductive age were presented either in advanced AIDS stage or CD4 less than 200 cells/uL (4788/5754 respectively), the ratio relative consistent annually for more than one decade.

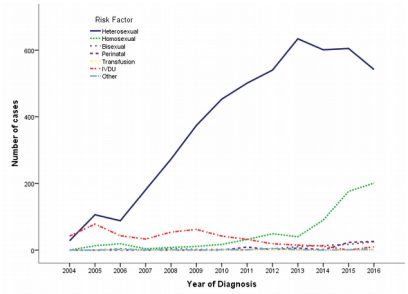

Figure 2. Risk factors for HIV transmission.

The median CD4 level showed improvement over the years with overall women appear to have higher level of CD4 than men (Figure 3). A Mann-Whitney U test revealed significant difference in median of CD4 of women (*Md* =167.00 cells/uL; range 0 – 1390 cells/uL) and men (*Md* = 60.00 cells/uL; range 0 – 1173 cells/uL), U = 785576; z = −11,8489; p = 0.00; r=0.21. Also significant difference in median CD4 of those in reproductive age 15 – 49 years (Md= 95.00 cells/uL; range 0 – 1390 cells/uL)) and non-reproductive age >49 years (Md=58.50 cells/uL; range 1 – 1173 cells/uL)), U= 20035; z= −3.48; p=0.00; r=0.06.

There was 83.5 percent (5119/6127) late testers; in which more than two-third were men (64.6 percent; 3307/5119) and within thereproductive age group (93.5 percent; 4788/5199). The proportion of late testers was lower in women groups (78.5 percent; 1812/2308) compared to men (86.6 percent;

3307/3819). Chi-square test for independence (with Yates continuity correction) indicated significant association between gender and late testers, X^2 (1, N=6127)= 67.81; p < 0.00; phi = 0.11.

The proportion of late testers was lower in reproductive age group (83.2%; 4788/5756) compared to non-reproductive age (88.7 percent; 331/373). Association between reproductive age and late testers was tested using Chi-square test for independence (with Yates continuity correction) indicated asignificant association between reproductive age and late testers, X^2 (1; N= 6127)= 7.39; p < 0.00; phi = −0.04.

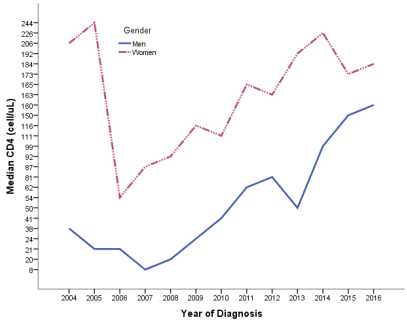

Figure 3. The median CD4 levels year 2004 – 2016.

Direct logistic regression was performed to assess the impact of gender and age group on the likelihood to present as late testers. The model contained two independent variables (gender and reproductive age groups). The full model containing all predictors was statistically significant, X^2 (2; N= 6127) = 73.34; p < 0.00, indicating that the model was able to distinguish between late testers new HIV seropositive and non-late testers.

The model as a whole explained between 1.2 percent (Cox and Snell R square) and 2.0 percent (Nagelkerke R squared) of the variance in late testers, and correctly classified 83.5 percent of cases. As shown in Table 2, all variable made a unique significant contribution to the model.

Table 2. Logistic regression predicting the likelihood presented as late testers *vs* non-late testers.

	B	SE	Wald	df	p	Odds Ratio	95% CI for Odds Ratio	
							Lower	Upper
Gender (Women)	0.562	0.070	65.316	1	0.000	1.754	1.531	2.010
Reproductive age (15 – 49 years)	0.411	0.168	5.961	1	0.015	1.508	1.084	2.098
Constant	-2.252	0.167	182.795	1	0.000	0.105		

The strongest predictor of the non-late tester was female with an odds ratio of 1.75. This indicated that women were almost two times more likely to present as non-late testers (CD4 > 200 cells/uL or no AIDS diagnosis during thestudy period or diagnosis of AIDS >12 months from HIV diagnosis) compared to men, controlling for age in the model. The odds ratio of 1.51 for reproductive age, indicating that reproductive age of 15 – 49 years were 1.5 times more likely to present as non-late testers compared to those with age > 49 years, controlling for another factor in the model.

4. Discussion

The latest UNAIDS data, covering 160 countries, demonstrated 36.7 million people living with HIV at all age by 2015. Among those, 1.9 million new infections were adults (15 and older) and 900.000 or 47 percent were women.[10] There were regional differences in new HIV infection among women and the proportion of women living with HIV as compared to men. The gaps even more remarkable at younger age group (age 15 – 44). In sub-Saharan Africa, women comprised 56 percent of new infections among adults (15 and older); and the proportion was higher among young women aged 15-

24, who made up 66 percent of new infections among young people. Data from Eastern Europe and Central Asia, women accounted for 31 percent of new HIV infections; however, among young women aged 15-24, the numbers reached 46 percent of new infections. In the Middle East and North Africa, women comprised 38 percent of newly infected adults; whereas young women aged 15-24 made up 48 percent of new infections. Whereas in Asia-Pacific, women accounted for 32 percent of new infections; as the numbers reached 41 percent among young women aged 15-24.[3,10] Indonesia data estimate that by 2015, 690.000 people were living with HIV; of those, of those 680.000 or almost 90 percent were adults and 250.000 or 37 percent were women.[11] Our study also showssimilar trend, where two-third or 37.7 percent people living with HIV were women. Among adults age 15 years or older, those within reproductive age contribute the most part. Reproductive age women and men who living with HIV have their specific needs and desires for reproductive health care. Prevention of sexually transmitted diseases, treatment,and care required by this group should be tailored and implemented toward target achievement of delaying HIV disease progression andavoiding HIV transmission.Multi-partner sexual behavior still becomes the main risk for HIV transmission from every part of the world as supported also by our study.[12]

The rate of late testers varies between countries and the CD4 cut-off definition for late testers. The United Kingdom, use the CD4 value of 350 cells/uL or less as for late testers, identified 40 percent of new cases in 2014 as late testers.[13] The European Centres for Disease Prevention and Control (ECDC) reported 49 per cents late testers (CD4 less than 350 cells/uL) in 2010.[14] The rate of late testers in our study was comparable with some countries in Latin America and the Caribbean (56 percent – 91 percent and Indian (83.37 percent).[15,16] The percentage of cases that considered as late testers; distinctly impact both prevention strategy and medical care services. The closeness of receiving AIDS diagnosis to initial HIV infection diagnosis represents missed opportunities for both prevention and medical care.[17] Patient diagnosed late in the course of HIV infection are more likely to transmit HIV to others because without treatment, the viral load will not be suppressed thus more infectious to other. They also more likely unaware of their HIV status and transmitting HIV without their knowledge.[18,19] Although free confidential testing is available throughout the Bali island, more than 90 percent of new HIV diagnosis qualified as late testers. Universal testing as part of routine health care is still not an endorsed practice. If we aim for minimizing missed opportunities for treatment, then early testing is mandatory.

The role of Indonesian women today is affected by multiple factors, namely modernization, globalization, improvement in education and advances in technology. In terms of gender equity, both man and women have their own portion of responsibility. Our study shows that women are not less vulnerable as for men anopportunity for HIV testing and medical care. The proportion of late tester was higher among men compared to women, also higher among older adult compared to those aged 15 – 49 years. The likelihood for presented as alate tester is higher in men compared to women and in those aged > 49 years compared to aged 15 – 49 years.

There are some limitations in our study: more variables would be beneficial if could be found, especially those that can measure social stigma and knowledge.

The results indicate that individual who might present late for HIV diagnosis and care, exist within all risk groups, age, and gender and possibly in any healthcare setting. We endorsed the need to ensure earlier identification and treatment of late testers by reviewing current strategies. Health care providers might also consider routine HIV testing in emergency unit, primary care, and all other healthcare facilities.

5. Conclusion

Women affected by HIV infection in almost equal number as for men. Most women and men diagnosed as late testers and within the reproductive age group. Women more likely to present as non-late testers compared to men and those within reproductive age also more likely to present as non-late testers.

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