

Correlation Linear Gingival Erythema, Candida Infection and CD4+ Counts in HIV/AIDS Patients at UPIPI RSUD Dr. Soetomo Surabaya, East Java, Indonesia

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Correlation Linear Gingival Erythema, Candida Infection and CD4+ Counts in HIV/AIDS Patients at UPIPI RSUD Dr. Soetomo Surabaya, East Java, Indonesia

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Abstract

East Java has been 2nd highest province with HIV/AIDS cases in Indonesia on 2013. Oral manifestations are among the earliest and most important indicator of HIV infection progression. Linear Gingival Erythema (LGE) is the one of seven oral manifestation which associated with HIV Infection. Clinical feature of LGE is a distinctive fiery red band along the margin of the gingiva. The etiology and pathogenesis of LGE are still questionable, but a candidal infection and decreased of CD4+ counts has been suggested.

The aim of this study was to investigate LGE with its correlation with Candida infection and decreased level of CD4+ in HIV/AIDS patient.

This study was an analytical observational research with cross-sectional and total sampling method. The samples consisted of 88 HIV/AIDS patients treated in UPIPI RSUD Dr. Soetomo Surabaya from July-August 2014 were recruited for Candida microbial screening on LGE lesion. Clinical specimens including oral swabs were collected. Diagnosed of LGE by clinical appearance, the oral cavity of research subjects examined by oral medicine specialist. CD4+ counts obtained from patient's medical record.

88 HIV/AIDS patients were examined, there were 7 cases (5,83%) LGE, 7 from 7 gingival margin found Oral Candidiasis (OC) (100%). LGE was found to be significantly correlated to OC and decreased CD4+ counts < 200 cells/mm³ ($p < 0.05$).

LGE related to candida infection and decreased CD4+ counts in HIV/AIDS patients.

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Introduction

Acquired Immune Deficiency Syndrome (AIDS) is a syndrome caused by Human Immunodeficiency Virus (HIV).¹ In recent years, HIV infection rates have been increased rapidly, many people were alive with HIV infection in the world.² East Java province was the second highest with HIV infection cases between 19,249 peoples and 8,976 peoples with AIDS infection.^{3,4}

RSUD Dr. Soetomo was the largest

hospital in eastern Indonesia as one of the tertiary referral hospitals in Indonesia. RSUD Dr Soetomo is one from seven hospitals that appointed by the Ministry of Health as a Pilot Project Services and HIV/AIDS Prevention since 2010 centered in *Unit Perawatan Intermediate Penyakit Infeksi* (UPIPI).⁵

Oral health is the important thing to identify quality systemic health of HIV/AIDS patients.⁶ HIV/AIDS patients have 60% to 90% oral manifestation as opportunistic infection.⁷ Detail history taking and examination the oral cavity of HIV/AIDS patients are important parts of the physical examination.⁸ Dentist must do a proper management of oral manifestation in HIV/AIDS to improve the Quality of Life (QoL). Medical clinicians must able to recognize HIV-associated oral disease.⁹

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Linear Gingival Erythema (LGE) also one of the seven oral manifestations that commonly associated with HIV infection. LGE referred as HIV/AIDS gingivitis is the most common form of HIV/AIDS-associated periodontal disease¹⁰. It is considered resistant to conventional plaque-removal therapies, being considered nowadays as lesion of fungal etiology. Some data indicate a relationship between LGE and colonization of Candida species that can be conclude that LGE is another variant type form candidiasis in HIV/AIDS patients¹¹. LGE characterized clinically by a red fired, linear band 2 to 3 mm wide on the marginal gingival accompanied by petechiae-like or diffuse red lesions on the attached gingival on the oral mucosa may be accompanied by bleeding¹². The prevalence of this lesion varies widely in different studies, ranging from 0 to 48%, although LGE was often misdiagnosed as chronic gingivitis marginalis¹³.

The aim of this study was to investigate LGE with its correlation with Candida infection and CD4⁺ counts in HIV-infected patient in UPIPI RSUD Dr. Soetomo 2014.

23 Materials and methods

This an analytical observational research with cross-sectional and total sampling method. All patients has been agreed to join this study by filled informed consent. This study was approved by the institutional ethics committee, RSUD Dr. Soetomo Surabaya (301/Panke. KKE/VI/2014 20 June 2014).

The samples consisted of 88 HIV/AIDS HIV seropositive patients treated in UPIPI RSUD Dr. Soetomo Surabaya from July-August 2014. Diagnosis of HIV infection have been done by Internal Medicine Department Tropic Disease Division and Clinical Pathology RSUD Dr. Soetomo Surabaya following the standard protocol at Integrated Counselling and Testing Centre that employs pretest and posttest counselling and filled informed consent before HIV testing. Three different rapid tests were used to detect HIV-1 and HIV-2 antibodies (CombAids (Span Diagnostics Ltd.), Retrocheck HIV (Qualpro Diagnostics), and Tri-Line (Rapid Diagnostics) following the manufacturer's instructions. CD4⁺ counts obtained from patient's medical record.

All the patients were recruited for Candida microbial screening. Clinical specimens including

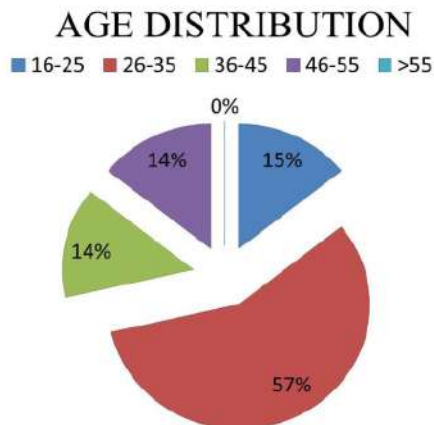
oral swabs were collected. Diagnosed of LGE by fungal test and clinical appearance, the oral cavity of research subjects examined by dentists specialized in Oral Medicine from Instalation of Dental and Oral Health, RSUD. Dr. Soetomo Surabaya and Department Oral Medicine, Faculty of Dental Medicine, Universitas Airlangga Surabaya

The samples were subjected to direct microscopy Potassium Hydroxide (KOH) preparation. In KOH-Calcofluorescent-stain method fungal characteristics like hyphae, yeast cells, and other fungal elements will fluorensce. Fungal culture was done on Sabouraud dextrose agar (SDA). Specimens were streaked and incubated at 37°C. Fungal growth was identified by colony morphology. Candida species identification based on carbohydrate utilization.

Correlation LGE, Candida Infection, and CD4⁺ counts was determined using Pearson's test with $p < 0.05$. Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) 17.0 software for windows 8.1 by SPSS Inc, Chicago, United State.

Results

In this study, there were 7 HIV/AIDS Patient with LGE cases (7.95%) associated with positive candida infection. Most of LGE cases can be found 26-35 years old patients group (57%) and most of them are male (86%) that can be seen in Figure 1, 2 and 3. In this study, there were Candida species in 7 LGE cases.



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Figure 1. Age distribution of HIV/AIDS patients with LGE.

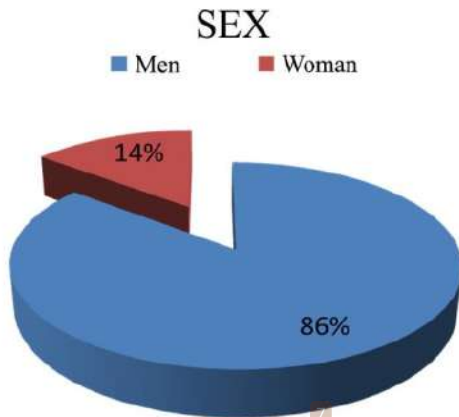


Figure 2. Sex distribution of HIV/AIDS patients with LGE.

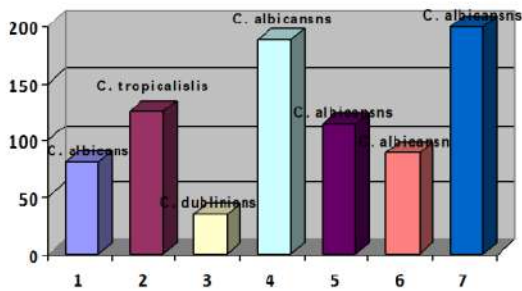


Figure 3. Candida species in seven LGE lesion with decreased CD4+ count $<200 \text{ cells/mm}^3$.

Most of them are *C. albicans* (71.43%) with decreased CD4+ count $<200 \text{ cells/mm}^3$, that can be seen in Figure 4. Pearson's Correlation Test showed that there was a correlation between the LGE and Candida infection on a significant level of 0,0092 ($p < 0.05$) and decrease of CD4+ counts on a significant level of 0,0045 ($p < 0.05$).



Figure 4. (A) 28 years old male, (B) 30 years old, (C) 35 years old, (D) 45 years old patients with LGE and OC, (E) 25 years old in fixed orthodontic treatment with LGE.

Discussion

HIV/AIDS is a serious universal health problem and most common example of an emerging infectious disease. Indonesia on 3rd highest country in Asia Pacific with the most widely HIV/AIDS cases, around 610.000².

The cases of LGE in this study are greater than the number that shown in previous study at UPIPI in 2011 found 5 cases of LGE (11%)¹². Periodontal lesion as oral manifestations tend to increase, it was not caused by plaque and calculus conditions but caused by immunodeficiency condition that occur in HIV/AIDS¹³.

LGE occur because of Candida infection in the subgingiva plaque. The microflora of LGE are similar with other periodontal lesions such as gingivitis and periodontitis¹⁴. The correlation of oral candidiasis and LGE were suspected. Microscopic examination of LGE shown *C. Dubliniensis* in 4 HIV/AIDS patient which had administered sytemic antifungal. The Etiology of LGE and its correlation with Candida infection are not clear yet.¹⁵

The previous study shown a subgingival plaque of HIV/AIDS patients with high viral load and low level of CD4⁺. *Saccharomyces cerevisiae* as the only fungal species that were detected in LGE, while *C. albicans* are not. *C. albicans* were detected in microbiology examination of LGE lesion from HIV/AIDS patients with low viral load and high level of CD4⁺¹⁶. The pathobiogenesis of LGE are unexplained yet¹⁷.

LGE mostly found in patients of HIV/AIDS with CD4⁺ < 200 cells/mm³¹³. The decrease of CD4⁺ lymphocytes cells cause decreased of imunne system and may cause the risk of opportunistic infection increased. This symptoms of opportunistic infections depend on the etiology of the infections^{17,18,19}.

There were significant correlation between LGE and OC ($p < 0,05$). The occurrence of Candida infection always associated with OC in patiens of HIV/AIDS. Candida actually comensal, but the decrease of sIgA (secretory Immunoglobulin A) and also the decrease of lymphocytes T cell become patogen²⁰.

In the previous study, *C. albicans* was the most frequent species found from the isolation in five from seven patients, which confirm that the main etiologic agent of oral candidiasis. A mixed

culture of *C. albicans* and *C. Tropicalis* confirmed the association with other species rather than *C. albicans* isolated from oral candidiasis. One patient exhibited positive growth for *C. dubliniensis* indicating that this species is also present. Previous study also demonstrated the presence of *C. dubliniensis* in subgingival of HIV-positive patients indicating that this species has emerged as another pathogen in vitro potential for azole resistance and enhanced adherence to human buccal epithelial cells^{15,18,21}.

Pathobiogenesis of OC strongly correlated with HIV/AIDS due to TAT (Trans-Activating Transduction or Activator Transcription) that have been produced in early cycle of viral replication^{22,23}. Interaction between HIV TAT protein with *C. albicans* cell's wall allows the transduction of gen that form specific pathway of hyphae (Hypal Spesific Genes, HSG)²⁴.

Conclusions

LGE has a significant correlation with Candida infection and decreased level of CD4+ counts in HIV/AIDS patients at UPIPI RSUD Dr Soetomo.

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