

## Management Of Oral Candidiasis Children And Infant With Hiv/Aids Infection : Report Of Two Cases

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### ABSTRACT

**Background:** HIV infection is characterized by progressive immunosuppression due to low absolute CD4 counts. The most common HIV-related oral disorder is oral candidiasis. First case, A 10-month-old baby girl complained of white plaque on her hard palate since 3 months ago. The patient had experienced the same before and was treated with Nystatin then the lesion resolved. The patient had HIV positive history and took Abacavir twice a day. The latest CD4 test was 3 months ago and the result was 1000 cells/ $\mu$ L. The second case, An 8-year-old male patient who complained white lesion in all over his mouth one week ago. The patient has been taking Nystatin 4 ml 4 times a day for 7 days but the lesion has not resolved. The patient had confirmed HIV at 2.5 years old and takes ARV regularly. The CD4 count three weeks ago was 8 cells/mm<sup>3</sup>. Both of them were diagnosed with acute pseudomembranous candidiasis

**Case:** The first patient was given Nystatin oral suspension 4 times a day and the lesion resolved gradually in 1 week. The caregiver instructed to clean the child's mouth with gauze and dipped in 0.12% Chlorhexidine Gluconate before using antifungal drugs. The second patient was given fluconazole 150 mg tablets 3-6 mg/kg once a day for 14 days. Both of the lesions responded well to antifungal.

**Conclusion:** Oral candidiasis in children with HIV often occurs in conditions of low CD4 and often appears as acute pseudomembranous candidiasis. Treatment of oral candidiasis in children is adjusted to the PNPk HIV Kemenkes RI 2019 according to the level of disease

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## INTRODUCTION

Human Immunodeficiency Virus (HIV) is a virus that attacks the body's immune system and causes a decrease in the immune system so that it is susceptible to other diseases or opportunistic infections. The condition of sufferers who experience other diseases due to HIV infection is Acquired Immunodeficiency Syndrome (AIDS).<sup>1</sup> HIV cases in children were first discovered in 1980.<sup>2</sup> The HIV virus is transmitted through several body fluids from infected people such as blood through blood transfusions, breast milk (breast milk), semen and vaginal fluids through sexual intercourse, and the use of needles, piercings, and tattoos that are not sterile.<sup>3</sup> HIV can also be transmitted from a mother to her child vertically during intrauterine, intrapartum, or post-natal (during breastfeeding). Vertical transmission serves as the main mode of transmission (92%) of HIV infection in children aged <13 years. Intrauterine transmission occurs by hematogenous spread across the placenta or by ascending infection to the amniotic fluid and membranes. Transmission during delivery occurs through mucocutaneous contact between the baby and the mother's blood, amniotic fluid, and cervicovaginal secretions as they pass through the birth canal. Transmission during labor can also occur through ascending infection from the cervix and maternal-fetal transfusions when the uterus contracts during labor.<sup>4</sup> Based on the latest data, HIV infects more than 2 million children aged less than 15 years in the world. In 2021, the number of HIV sufferers in Indonesia will reach 29,900 people. Of the total cases, 0.7% occurred in children under 4 years of age, 1.3% aged 5-14 years, 7.2% aged 15-19 years, 16.3% aged 20-24 years, and the most 71, 3% in the age group of 25-49 years. Children with HIV are more dangerous because children's immune systems are not yet fully formed and they

are immunosuppressed, causing the disease to develop more quickly.<sup>5</sup>

Oral candidiasis or oral thrush is an opportunistic infection that manifests in the oral cavity caused by HIV infection. *Candida* which is a yeast-like fungus is the cause of oral thrush. In healthy people, *Candida albicans* is a normal flora of the oral cavity. In immunodeficiency states, *Candida albicans* can overgrow and cause discomfort, loss of sense of taste, and dysphagia.<sup>7</sup> Oral candidiasis appears as white plaque lesions adhering to the oral mucosa such as the buccal mucosa, tongue, palate, gingiva, and oropharynx. The white plaque can be removed by wiping it but it will hurt and bleeding usually occurs.<sup>8</sup> This article aimed is to report of two cases of management oral candidiasis in children and infants with HIV.

## CASE 1

A 10-month-old baby girl with her mother came to RSIGM Sultan Agung, Semarang with complaints of white plaque on her child's palate since 3 months ago. It is not painful. The patient had experienced the same lesion before and was treated with Nystatin then the lesion resolved. The patient had HIV positive history and taking Abacavir twice a day. The latest CD4 test was 3 months ago and the result was 1000 cells/ $\mu$ L. Now, the patient was cough and mild fever, so the patient had Ambroxol, anti-fever, Domperidone, and vitamins from the physician. The patient had no history of food or drug allergies. The patient's biological mother was confirmed HIV positive 1 month ago. Extraoral examination showed no swollen lymph nodes. Intraoral examination showed multiple white plaques, which can be scrapped off, well-demarcated, with a reddish area. The diagnosis was Oral Candidiasis e.c. HIV. The therapy was carried out by giving Nystatin Oral Suspension for times a day. Patient education includes cleaning the

plaques using gauze and warm water regularly, always sterilizing bottles and pacifiers, adequate nutrition, and taking medicine as prescribed.

1 week later, the white plaques already disappear but still a mild lesion left. Patient is in good general condition. Extraoral examination showed no swollen lymph nodes. An intraoral examination there were still white plaques on the hard palate. At this visit, the patient was instructed

to continue medication with Nystatin Oral Suspension dripped 4 x 1 mm on white plaque lesions on the hard palate. Patients were given education to keep using the drug regularly, if using a pacifier it had to be sterile, and the patient's mother was instructed to clean the whites on the roof of her child's mouth with gauze and dipped in 0.12% Chlorhexidine Gluconate before using antifungal drugs, as well as control 1 week later. The lesion resolve totally within 2 weeks.



**Figure 1.** Clinical feature at hard palate showed white plaque (A) 1<sup>st</sup> visit (B) 2<sup>nd</sup> visit (1 week later)

## CASE 2

An 8-year-old male patient came to RSIGM Sultan Agung Semarang complaining white lesion one week ago. It is painful and the patient has difficulty eating. The patient has been taking Nystatin 4 ml 4 times a day for 7 days but the lesion has not resolved. The patient had confirmed HIV at 2.5 years old and takes ARV regularly. The patient weighs 17 kg, has had diarrhea since one week ago, and the CD4 count three weeks ago was 8 cells/mm<sup>3</sup>. The patient has an allergy to Amoxicillin. The patient's father, mother, and younger brother were confirmed to be HIV/AIDS.

Extraoral examination revealed no abnormalities. Intraoral examination results showed white pseudomembrane lesions on the right, left buccal, anterior lingual, hard palate, and labial mucosa (Figure 2) Patient was diagnosed clinically with oral candidiasis.

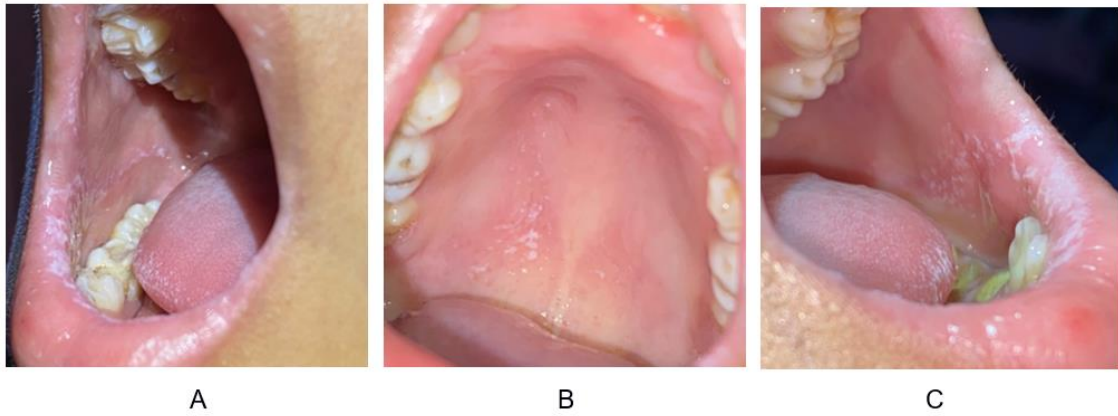
The patient was prescribed Fluconazole 150 mg which was taken ½ tablet once a day for 7 days, multivitamins once a day, and Chlorhexidine gluconate mouthwash 3 times a day. Patients were instructed to take medication regularly, maintain oral hygiene, and consume adequate nutrition. Lesion swabbed and sent to microbiology laboratory for cultured

1 week later, the patient admitted that the lesions resolved and not complained painful anymore. However, there were reddish band-shaped lesions on the upper and lower anterior maxillary gingiva of (Figure 3). The results of the microbiology test showed the presence of *Pseudomonas aeruginosa* bacteria colonies.

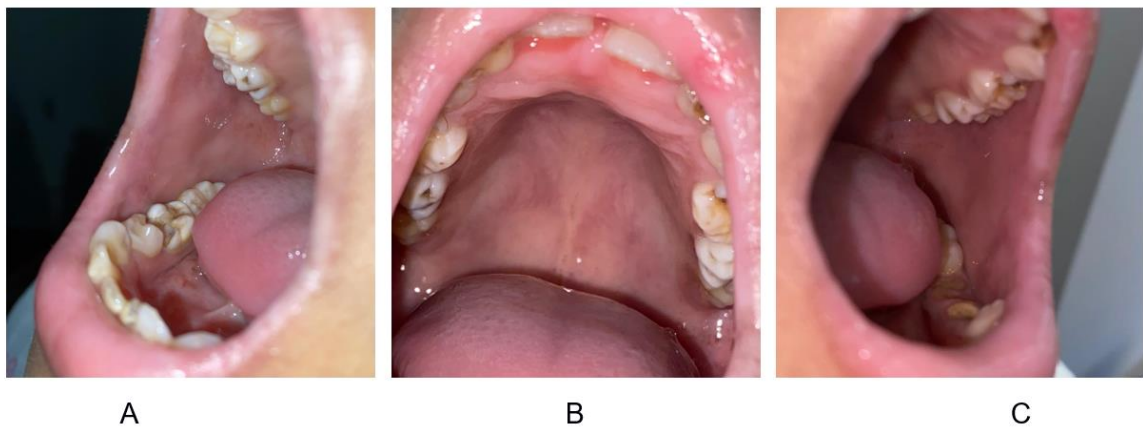
Follow-up treatment is carried out by continuing to use Fluconazole, mouthwash, and multivitamins for one week. Guardians of patients are given education to clean the patient's oral cavity

with gauze and given mouthwash. In the next visit, the lesion was completely resolved, and an intraoral

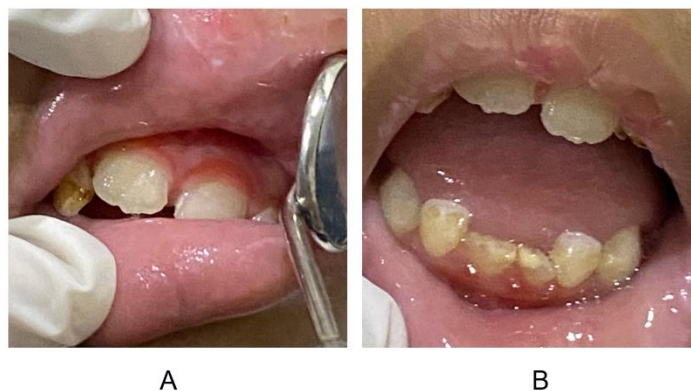
examination showed no lesions on the oral cavity, so the treatment was stopped.



**Figure 2.** Clinical feature of 2<sup>nd</sup> patient at 1<sup>st</sup> visit showed white pseudomembranous that can be scrapped off with mild erythema in the (A) right buccal mucosa (B) hard palate (C) left buccal mucosa



**Figure 3.** Clinical feature of 2<sup>nd</sup> patient at 2<sup>nd</sup> visit (1 week later) showed white pseudomembranous that can be scrapped off with mild erythema in the (A) right buccal mucosa (B) hard palate (C) left buccal mucosa



**Figure 4.** Clinical feature of 2<sup>nd</sup> patient at 3<sup>rd</sup> visit showed more diffuse erythema in marginal gingiva in the (A) maxillary central incisor (B) mandibular central incisor

## DISCUSSION

Pseudomembranous oral candidiasis/oral thrush is the most prevalent soft tissue lesion in children with HIV infection (reported in roughly 75% of cases). Erythematous Candidiasis and angular cheilitis are also frequent in HIV-infected children. A variety of factors may influence a child's candidiasis risk.<sup>7</sup> Feeding habits and nutritional requirements that increase the frequency of fermentable carbohydrate intake (e.g., formula, juices, milk, dietary supplements), especially when supplied with bottles, promote candidiasis growth. Beginning at birth, mouth rinsing, nutritional and medication management, and washing the entire mucosal and gingival tissue area may assist to control oral candida and prevent the progression of oral candidiasis. Oral hygiene instructions should be given to both children and caregivers.<sup>8</sup>

The virulence of candida in the oral cavity has a growth journey from yeast to hyphae. Initially, yeast in candida fungi produces adhesin agglutinin like sequence (ALS) and hyphal wall protein (HWP1) to adhere to the surface of the host epithelium. The adhesion that is formed will be stronger and result in changes in the form of yeast into hyphae by thigmotropism. Candida fungi with their hydrolytic enzymes will produce secreted aspartyl proteinase (SAP) which has the ability to destroy host cell barriers, facilitate penetration, provide a nitrogen source, increase adhesion to host cells, and decrease immunoglobulins and other defense proteins. SAP candida has ten types, SAP1 - SAP8 are secreted extracellularly, while SAP9 and SAP10 are membrane bound. SAP1 and SAP3 affect the formation of candida colonies, while SAP4 - SAP6 function to stimulate hyphal growth. The attachment of candida will develop into a biofilm with yeast at its base while the hyphae are on the outermost part of the biofilm. Factors that

influence the pathogenesis of candida fungi include stress response by heat shock protein (HSP), automatic hyphae formation by absorption of amino acids, ammonia excretion, extracellular alkalization, absorption of various carbon and nitrogen compounds, and absorption of metals such as iron.<sup>9,10</sup>

In the first patient, In this patient, objective examination at the first appointment revealed a white plaque on the palate that could be removed and left erythema area, suggesting an oral candida yeast infection. The patient's mother complained that the lesion had existed since 1 month before the first visit. Antifungal drugs used to treat candidiasis are divided into several categories, namely: polyenes (nystatin and amphotericin B); Azole ergosterol biosynthesis inhibitors (miconazole, clotrimazole, ketoconazole, itraconazole and fluconazole), allylaminethiocarbamates, and morpholines; and the DNA analogue 5-fluorocytosine, and caspofungin.<sup>11</sup> The choice of antifungal treatment depends on the lesion and the patient's immunological status. There are three main targets of antifungal drugs for Candida, cell membrane, cell wall, and nucleic acids. Administration of polyene antifungal drugs is recommended for mild cases, while for moderate-severe cases Azole-type drugs are given. Topical antifungal drug classes used in candidiasis include imidazoles and polyenes. Polyene is a fungicide drug that works by binding directly to ergosterol in the fungal cell membrane, causing leakage of cytoplasmic contents which causes fungal cell death. Nystatin or amphotericin B solutions are used for 4 weeks. Systemic antifungals are usually indicated in cases of disseminated disease and/or in patients with compromised immune systems. Azoles are fungistatic drugs that inhibit the fungal enzyme lanosterol demethylase which is

responsible for the synthesis of ergosterol.<sup>12</sup> In using nystatin suspension, Patil S et al., claim that the dose of nystatin suspension is 400,000 - 600,000 units, four times daily, for seven to fourteen days. Based on PNPk HIV 2019 antifungal administration for oral candidiasis in children, namely For mild cases: nystatin suspension (100,000 U/mL) 4 x 1-4 mL for 7-14 days. For moderate-severe cases: oral fluconazole 3 mg/kg/day for 7-14 days.<sup>4</sup> In this patient, given Nystatin Oral Suspension 4x1 ml.

In the second patient, objective examination at the first meeting revealed pseudomembranes on the palate, lingual, buccal, and labial areas indicating an oral candida yeast infection. In addition, the diagnosis is made by conducting a culture swab. Examination of the culture swab did not show any *Candida* fungal colonies but showed the presence of *Pseudomonas aeruginosa* bacteria colonies. *Pseudomonas aeruginosa* is a gram-negative bacterium which is a normal flora of the oral cavity, but can be pathogenic when a person's immune state is compromised. These bacteria are the cause of the clinical picture of linear gingival erythema. Anamnesis on the second visit the patient had no complaints of pain in the oral cavity. Objective examination showed no pseudomembrane lesions in the patient's oral cavity, but linear gingival erythema was found on the free gingival margins of the upper and lower anterior teeth. Objective examination, subjective examination, and patient investigations showed that the patient was in category 3 (CD4 <200 cells/mm<sup>3</sup>),<sup>13</sup> where the patient had clinical manifestations such as diarrhea, fever, oral candidiasis, drastic weight loss, bacterial infection, gingivitis, and the last patient's CD4 count was 8 cells/mm<sup>3</sup>. Linear gingiva erythema is a disease that can be found in HIV patients. This situation is the initial state of Necrotizing Ulcerative

Periodontitis. The etiology is the colonization and growth of anaerobic gram-negative bacteria which are often found in the oral cavity. The clinical appearance of linear gingival erythema is a reddish band that follows the contour of the free gingival margin. These reddish lesions do not significantly change the shape and size of the gingiva, but will spontaneously bleed on probing.<sup>14</sup> Nugraha et al said that so far there is no definite correlation between oral candidiasis and linear gingival erythema. Nugraha et al stated that HIV/AIDS patients with low CD4 counts and high viral loads have subgingival plaque containing the same bacteria as the bacteria that cause LGE. Meanwhile, *C. albicans*, which is the cause of oral candidiasis, is not a microorganism that causes LGE. The differential diagnosis of LGE is marginal gingivitis, in which patients with marginal gingivitis have a clinical picture of inflammatory gingiva, discoloration, size, consistency, and unstippling gum surface shape. The cause of this condition is the accumulation of plaque bacteria in the subgingiva.

Treatment of LGE in this patient is to maintain oral hygiene by giving the correct toothbrush instructions and using chlorhexidine gluconate mouthwash 3 times a day which functions as an antiseptic and astringent.<sup>15</sup> Oral candidiasis in patients given treatment based on the principles of pediatric HIV management, namely administration of Nystatin 400,000–600,000 units 4-5 times per day, evaluated for one week. If nystatin has been administered and there is no positive response, oral fluconazole 150 mg tablets are administered at an oral dose of 3-6 mg/kg once a day for 14 days. Therapy for the AIDS condition in this patient is the consumption of ARVs at a dose of ½ tablet 2 times a day. The purpose of giving ARVs is to suppress the development of HIV replication in cells. If there is a decrease in the amount of HIV

virus in the patient's body, opportunistic infections can also be handled properly.<sup>16</sup>

Dentists must provide education about the importance of maintaining the oral health of pediatric HIV patients by paying more attention to and cleaning up leftover food and medicines in the oral tissues. Preventive measures to prevent further infections in the oral cavity can be carried out with cariogenic medication management, sealants, systemic and topical administration of fluoride, reducing high-carbohydrate foods, and child nutritional management.<sup>17</sup>

## CONCLUSION

Oral candidiasis in children with HIV often occurs in conditions of low CD4 and often appears as acute pseudomembranous candidiasis. Treatment of oral candidiasis in children is adjusted to the PNPk HIV Kemenkes RI 2019 according to the level of disease, besides that it is necessary to maintain the body condition of children with HIV through environmental hygiene and equipment, adequate nutrition, and routine consumption of ARVs. Dentists must provide education on how to maintain oral health in pediatric patients with HIV

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