Predictor and Saverity Caries in HIV/AIDS Patient and Relationship with Antiretroviral Therapy (ARV)

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ABSTRACT

Clinical findings about the adverse effects of the use of antiretroviral drugs in the oral cavity of people with HIV / AIDS began to be found. A case regarding the side effects of the use of antiretroviral drugs is the discovery of oral cavity lesions in the form of whitish plaque on the lips and right buccal mucosa that has occurred more than one month accompanied by complaints of taste disorders, xerostomia, and a burning feeling in the mucosa of patients using Nevirapine, Zidovudine and Lamivudine. This study was to analyze the relationship of anti-retroviral treatment in HIV AIDS sufferers to caries predictors, and caries severity, and analyze the relationship between the duration of antiretroviral treatment to caries predictors and caries severity. This study used an observational method with cross sectional or cross sectional design by conducting direct observations, on 100 samples of HIV / AIDS sufferers using anti-retroviral drugs at the Yayasan Peduli Kelompok Dukungan Sebaya (YPKDS) Makassar held in October 2019. Data were analyzed with chi square test.

The results obtained that there is a relationship between antiretroviral treatment in HIV / AIDS patients with caries predictors ($p = 0.357$) and caries severity ($p = 0.005$), while analysis of the duration of antiretroviral treatment is less than 5 years and more than 5 years there is no relationship with caries predictors ($p = 0.730$) and caries severity ($p = 0.428$).

KEYWORDS: Antiretroviral, Caries Predictor, Caries Severity

ARTICLE DETAILS

1. INTRODUCTION

AIDS stands for Acquired Immune Deficiency Syndrome, which is a decrease in the body's resistance to various diseases due to infection with the HIV virus (Human Immunodeficiency Virus). Someone who is infected with HIV can easily be attacked by various other diseases due to low immunity and can result in death. HIV, which is the cause of AIDS, has a primary target cell, T4 lymphocyte cells, which have CD4 receptors. HIV infects in a way, the 120 HIV sheath protein will touch and bind to the host cell's CD4 receptor, then the virus replicates, starting with the production of the same pro viral RNA so that new virions will form, a new HIV virus ready to infect the target cell another, after exiting the host cell through budding. After the experts discovered that AIDS was caused by HIV, various studies about drugs that could eliminate this virus began. Drugs used in HIV virus therapy are antiretroviral drugs [1].

HIV / AIDS attacks the immune system of the human body, causing a decrease in endurance in the body, and as a continuation of the effects of the attack there will be a variety of abnormalities both by the condition of the immune system and by various opportunistic diseases. Some of these opportunistic disorders / diseases also occur in the oral cavity and certainly have clinical manifestations in the human oral cavity [2].

Currently the most well-known antiretroviral drug administration technique is Highly Active Antiretroviral Therapy (HAART), which has brought revolutionary changes to the treatment and prognosis of HIV and AIDS for those who can benefit from the treatment. HAART is a combination

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of antiretroviral agents namely Reverse Transcriptase Inhibitors and Protease Inhibitors. This therapeutic strategy provides very significant results in reducing disability, the prevalence of some oral lesions and deaths caused by HIV infection. Therefore HAART can increase the life expectancy of HIV patients. Although the use of HAART can increase patient life expectancy, but the main problem that must be taken into consideration is the adverse effects of the use of this drug, especially the problems it causes in the oral cavity [3].

Some clinical findings of adverse effects due to the use of antiretroviral drugs in the oral cavity of people with HIV / AIDS began to be found. A case regarding the side effects of the use of antiretroviral drugs was reported by Moura, et al, namely the discovery of oral cavity lesions in the form of whitish plaque on the lips and right buccal mucosa that has occurred more than one month accompanied by complaints of taste disorders, xerostomia, and a burning feeling in the patient's mucosa which uses Nevirapine, Zidovudine, and Lamivudine [3].

Another case was also reported by Liza Meutia Sari et.all, who found Stevens-Johnson Syndrome (SSJ) in a patient using combination antiretroviral drug therapy consisting of Duvival (Zidovudine 300 mg and Lamivudine 150 mg) and Neviral (Nevirapine 100 mg) twice a day [4].

Dental caries is a chronic regressive process that begins with the dissolution of enamel minerals as a result of disruption of the balance between enamel and its surroundings caused by the formation of microbial acids from the substrate so that the destruction of organic components arises which eventually results in cavity. There are 3 main factors that play a role, namely the host factor, agent (microorganism), substrate (diet) and plus the time factor, which is described as three overlapping circles for caries, then the condition of each of these factors must be vulnerable host, cariogenic microorganisms, suitable substrate and long time .

2. METHODS

This study used an observational method with a cross sectional design by directly observing the predictors and severity of dental caries in 100 samples of HIV AIDS sufferers using anti-retroviral drugs at the Yayasan Peduli Kelompok Dukungan Sebaya (YPKDS) Makassar. The study was conducted in October 2019. Data retrieval lasted for 6 days. To detect the possibility of dental caries or caries predictors, caries detectors are used in the form of Any Seek ^{TM} red dye. After cleaning all visible caries tissue, apply 1 drop of Any Seek to the cavity and wait 5-10 seconds, then wash and dry. Red areas indicate carious dentin. To examine the relationship of anti-retroviral treatment with caries predictors and caries severity in HIV AIDS patients in YKPDS Makassar, the chi square test was used, as well as to see the time relationship with the 2 variables the chi square test was used.

3. RESULT

Table 1. Relationship between duration of drug use and type of drug against caries predictors

Duration of Use	Type of ARV	Caries Predictors								total
		no teeth	1 tooth	2 teeth	3 teeth	4 teeth	5 teeth	7 teeth	11 teeth	
Less than 5 years	Defural	6	1	1	1	1	2	0	0	12
	FCD	22	8	4	3	1	0	0	1	39
	HRV	4	0	0	0	0	0	0	0	4
	Nefiral	0	1	0	0	1	0	0	0	2
	V-Tripel	2	0	0	0	0	0	0	0	2
	Total	34	10	5	4	3	2	0	1	59
More than 5 years	Defural	14	3	1	0	0	3	1	0	22
	FCD	5	1	1	0	1	1	0	0	9
	Nefiral	4	0	1	0	1	0	0	0	6
	V-Tripel	2	0	1	0	1	0	0	0	4
	Total	25	4	4	0	3	4	1	0	41
Total	Defural	20	4	2	1	1	5	1	0	34
	FCD	27	9	5	3	2	1	0	1	48
	HRV	4	0	0	0	0	0	0	0	4
	Nefiral	4	1	1	0	2	0	0	0	8
	V-Tripel	4	0	1	0	1	0	0	0	6
	Total	59	14	9	4	6	6	1	1	100

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Table 1 shows that the number of patients who had caries predictors without dental caries was 59 people with 34 years of drug use longer than 34 years and 25 years more than 5 years. The number of patients without caries teeth who consumed Defural with a duration of less than 5 years was 6 people, FCD was 22 people, HRV was 4 people, and V-triple was 2 people. The number of patients without caries teeth who consumed Defural with a duration of more than 5 years was 14 people, who consumed FCD for 5 people, nephiral for 4 people, and V-triple for 2 people.

The number of patients who have a predictor of 1 dental caries as many as 14 people with a duration of drug use of less than 5 years by 10 people and more than 5 years by 4 people. The number of patients who have a predictor of 1 dental caries who consumed Defural with a duration of use of less than 5 years was 1 person, who consumed FCD as many as 8 people, and nephiral as much as 1 person. The number of patients who had a predictor of 1 carious tooth who consumed Defural with a duration of use of more than 5 years was 3 people, and who consumed FCD as many as 1 person.

The number of patients who had predictors of 2 caries teeth was 9 people with a duration of drug use of less than 5 years by 5 people and more than 5 years by 4 people. The number of patients who had predictors of 2 caries teeth who consumed Defural with a usage time of less than 5 years was 1 person, and FCD was 4 people. The number of patients who had predictors of 2 caries teeth who consumed Defural with a duration of more than 5 years was 1 person, who consumed FCD as much as 1 person, nephiral as much as 1 person, and V-triple as much as 1 person.

The number of patients who had predictors of 3 caries teeth was 4 people with a duration of drug use of less than 5 years as many as 4 people.

The number of patients who had predictors of 4 caries teeth was 6 people with a duration of drug use of less than 5 years as many as 3 people and more than 5 years as many as 3 people. The number of patients who had predictors of 4 caries teeth who consumed Defural with a duration of use of less than 5 years was 1 person, FCD was 1 person, and nephiral was 1 person. The number of patients who had predictors of 4 carious teeth who consumed FCD with a duration of use of more than 5 years was 1 person, who consumed nephiral by 1 person, and V-triple by 1 person.

The number of patients who have a predictor of 5 caries teeth as many as 6 people with a duration of drug use of less than 5 years by 2 people and more than 5 years by 4 people. The number of patients who had predictors of 5 caries teeth who consumed Defural with a duration of use of less than 5 years was 2 people. The number of patients who had predictors of 5 caries teeth who consumed Defural with a duration of use of more than 5 years was 3 people, and consuming FCD as much as 1 person.

The number of patients who have a predictor of 7 caries teeth is 1 person with a duration of drug use of more than 5 years and the drug consumed is Defural. The number of patients who had a predictor of 11 caries teeth was 1 person with a drug duration of less than 5 years and the drug consumed was FCD.

Table 2. The relationship between duration of drug use and type of drug on caries severity

Duration of Use	Type of ARV	Severity of Caries			Total
		No damage	Not severe	Severe	
Less than 5 years	Defural	3	4	5	12
	FCD	3	16	20	39
	HRV	1	2	1	4
	Nefiral	1	1	0	2
	V-Tripel	0	0	2	2
	Total	8	23	28	59
More than 5 years	Defural	3	2	17	22
	FCD	3	1	5	9
	Nefiral	1	0	5	6
	V-Tripel	0	1	3	4
	Total	7	4	30	41
Total	Defural	6	6	22	34
	FCD	6	17	25	48
	HRV	1	2	1	4
	Nefiral	2	1	5	8
	V-Tripel	0	1	5	6
	Total	15	27	58	100

Table 2 shows that the number of patients who did not have caries damage was 15 people with a duration of drug use less than 5 years as many as 8 people, and more than 5 years as many as 7 people. The number of patients who did not have caries damage who consumed Defural with a duration of less than 5 years was 3 people, who consumed FCD by 3 people, HRV by 1 person, and nephiral by 1 person. The number of patients who did not have caries damage who consumed Defural with a duration of use of more than 5 years was 3 people, who consumed FCD by 3 people, and nephiral by 1 person.

The number of patients who have caries is not severe as many as 27 people with a duration of drug use of less than 5 years as many as 23 people and more than 5 years as many as 4 people. The number of patients who had non-severe caries who consumed Defural with a duration of less than 5 years was 4 people, who consumed FCD for 6 people, HRV for 2 people, and nephiral for 1 person. The number of patients who have non-severe caries who consumed Defural with a duration of use of more than 5 years was 2 people, who consumed FCD for 1 person, and V-triple for 1 person.

The number of patients who have severe caries as many as 58 people with a duration of drug use of less than 5 years as many as 28 people and more than 5 years as many as 30 people. The number of patients who have severe caries who consumed Defural with a duration of less than 5 years was 5 people, who consumed FCD as many as 20 people, HRV as many as 1 person, and V-triple as many as 2 people. The number of patients who had severe caries who consumed Defural with a duration of more than 5 years was 17 people, who consumed FCD as many as 5 people, Nefiral as many as 5 people, and V-triple as many as 3 people.

Table 3. Chi square test the relationship of ARV types with salivary PH, caries predictors, plaque indexes, and caries severity

Type of ARV	Variable	p-Value	Information
Defural	Caries Predictors	0,559	No significant
	Severity of Caries	0,049	Significant
FCD	Caries Predictors	0,331	No significant
	Severity of Caries	0,037	Significant
HRV	Caries Predictors	-	Undefined [*]
	Severity of Caries	-	Undefined [*]
Nefiral	Caries Predictors	0,149	No significant
	Severity of Caries	0,048	Significant
V-Tripel	Caries Predictors	0,472	No significant
	Severity of Caries	0,439	No significant
Total	Caries Predictors	0,357	No significant
	Severity of Caries	0,005	Significant

Note: (*) the data is constant so it cannot be tested for chi square

Table 3 shows that the p-value of the caries severity variable is 0.049 less than 0.05. So it can be concluded that the type of Defural has a significant relationship to the caries severity variable. The p-value of the caries severity variable is 0.037 less than 0.05. So it can be concluded that the type of FCD has a significant relationship to the caries severity variable. The p-value of the caries severity variable is 0.043 and 0.048 less than 0.05. So it can be concluded that the type of Nefiral has a significant relationship with the severity of caries.

The overall total p-value of the caries predictor variable is greater than 0.05. So it can be concluded that the whole type of ARV did not have a significant relationship to the caries predictor variable. The overall total p-value of the caries severity variable is 0.005 less than 0.05. So it can be concluded that the whole type of ARV has a significant relationship to the caries severity variable.

Table 4 Chi square test the relationship between duration of use with caries predictors and caries severity

Duration of Use	Variable	p-Value	Information
Less than 5 years	Caries Predictors	0,403	No significant
	Severity of Caries	0,376	No significant
More than 5 years	Caries Predictors	0,832	No significant
	Severity of Caries	0,634	No significant
Total	Caries Predictors	0,730	No significant
	Severity of Caries	0,428	No significant

Table 4 shows that the p-value of the variable, caries predictor, and caries severity is greater than 0.05 so it can be concluded that the duration of drug use is less than 5 years and more than 5 years has no significant or unrelated relationship to, caries predictor, and caries severity.

The p-value of the caries predictor variable is smaller when the duration of use is less than 5 years than the length of use of more than 5 years. The p-value of the variable caries severity is smaller when the duration of use is less than 5 years than the length of use of more than 5 years.

4. DISCUSSION

Antiretroviral drugs, can cause xerostomia in people with HIV AIDS is a predisposing factor for caries. The exact cause of the occurrence of xerostomia in HIV patients is unknown, but from some of the side effects of antiretroviral drugs, fat infiltration in the parotid gland may be one of the things that can cause this, due to enlargement of the parotid gland which is likely to disrupt salivary flow [5]. Xerostomia is a condition where saliva cannot function properly, causing the mouth to become dry. Xerostomia can be caused by various things such as drug side effects, complications of the disease and infection, dehydration, radiation therapy and surgery to clean the salivary glands. Antiretrovirus is one drug that gives xerostomia side effects. Antiretroviral drugs that can give xerostomia side effects are Didadosine, Efivarenz, Indinavir, Nelfinavir, Ritonavir and Saquinavir [3][6] [7].

Saliva is a complex oral fluid that consists of a mixture of secretions from large and small salivary glands present in the oral mucosa. Saliva is able to liberalize early caries because it still contains a lot of calcium and phosphate ions. The ability of saliva to remineralize is increased if the fluorine ion. Besides affecting the pH, therefore, if salivary flow decreases or disappears, caries might not be controlled [8]. Saliva is the first defense against caries disease, besides it also functions as a lubricant, protective, buffering, cleaning, anti-solvent and anti-bacterial. However, saliva also plays another important role, namely in the process of dental plaque formation, saliva is also a good medium for the life of certain microorganisms associated with dental caries [9].

Prolonged xerostomia condition causes reduced salivary function and increased cariogenic bacteria, causing caries to increase and in this study significant caries severity was seen in HIV AIDS patients taking antiretroviral drugs [10]. While the steps to predict caries with chemicals that are safe are not significant due to the stage of demineralization due to acidity of the oral cavity can be slowed down with the awareness of patients in YKPD often get delivery and health consultation about how to care for oral health.

Antiretroviral treatment in people with HIV / AIDS has a relationship with predictor caries (p= 0,357) and caries severity (p=0.005). Duration of antiretroviral treatment in

people with HIV / AIDS is not associated with predictors of caries, and caries severity.

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This Study is in line with Ponnam Et.al's who research to 95 children in India with HIV AIDS states that manifestations of HIV that were observed in children receiving HAART include dental caries (26%), periodontal diseases (23%), candidiasis (19%), hyperpigmentation (17%), ulcerative stomatitis (9%) and one case of mucocele [11].

From the long-term side of antiretroviral use both caries predictors and caries severity are not significant, but all consumption less than 5 years gives a smaller p value, this means there are other factors compared to the terms of use which is more closely related. This factor is primarily a condition of xerostomia due to retroviral consumption which must be used every day and forever.

Research conducted by Rezaei-Soufi et al., 2014 of 100 people with HIV in Kermanshah, Iran shows results highly active antiretroviral therapy cannot be considered a single factor in prevalence of dental caries in patients with HIV infection. However, more research is recommended to assess the cariogenic potential of these drugs [12].

Research conducted by Nugraha et al (2019) on 29 children aged 1-12 years with HIV at Dr. General Hospital Soetomo Surabaya shows that the prevalence of caries in children suffering from HIV / AIDS is very high at 86.2 percent with the dmft / DMFT caries index 8.2 / 6.3. There is a significant correlation between the low CD4 + count and the high prevalence of caries [13].

This research is not in line with research conducted by Kalanzi et al (2019) on

748 participants with duration on antiretroviral < 2 years 4.8 ± 4.4, > 2 years but < 5 years 5.7 ± 5.5, > 5 years 6.6 ± 6.0 $p < 0.05$) in HIV care clinic in Uganda shows that duration of antiretroviral was associated with increased risk and severity of caries. Therefore, they recommend integration of dental care in HIV treatment programs [14].

5. CONCLUSION

Antiretroviral treatment in people with HIV / AIDS has a relationship with predictor caries (p= 0,357) and caries severity (p=0.005). Duration of antiretroviral treatment in people with HIV / AIDS is not associated with caries predictors (p = 0.730) and caries severity (p = 0.428)

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