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Association Between Antiretroviral Therapy Adherence and Viral Suppression Among People Living with HIV in Bogor City: A Case-Control Study

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ABSTRACT

Human Immunodeficiency Virus (HIV) continues to be a major global public health problem. HIV requires Antiretroviral (ARV) treatment to suppress the amount of HIV virus in the body. Adherence to ART can be influenced by a number of factors, including the patient's social situation and clinical condition, the prescribed regimen, and the patient-provider relationship. Adherence to ARV treatment is essential for PLWHA to achieve treatment success. Conversely, non-adherence to treatment can result in virologic failure. Virologic failure is an early sign of treatment failure. Over time, virologic failure will be followed by immunologic failure and ultimately clinical failure will occur. The purpose of this study was to determine the relationship between adherence to antiretroviral therapy and viral suppression in HIV patients in Bogor City. Research Methods This study is a quantitative study using an analytical observation method with a case-control study design. The study population was all people with HIV recorded in SIHA version 1.7 in Bogor City. The sampling technique used total sampling for the case group and simple random sampling for the control group. Data were taken from viral load examinations on a sample of 84 people and controls 3 times more than the number of cases, namely 252 people. The results of the study showed a significant relationship between adherence to antiretroviral therapy and viral suppression in HIV sufferers in Bogor City with a large association of 13.39 (95% CI: 6.09 - 29.41, p value: 0.000). Conclusion People with HIV in Bogor City who do not experience viral suppression have a low level of adherence with a proportion of 34.52% greater than in the group of people with HIV who experience viral suppression with a proportion of only 5.16% at the same level of adherence..

Keywords : HIV; Antiretroviral Therapy; Compliance; Viral Suppression; Case-Control Study.

INDTRODUCTION

HIV continues to be a major global public health problem. The death toll reached 40.1 million. In 2021, 650,000 people died from HIV-related causes, and 1.5 million people were infected with HIV. An estimated 38.4 million people were living with HIV at the end of 2021, two-thirds of whom, 25.6 million, were in the WHO African Region [1]Global access to antiretroviral (ARV) and treatment success indicate that approximately 85% of people living with HIV know their HIV status, but only 75% access treatment, and 68% have viral suppression, meaning that approximately 32% have not yet achieved viral suppression [2]Indonesia has a complex HIV epidemic pattern, spread across a wide area and with a large population, which presents unique challenges in HIV control. Spectrum modeling results in Indonesia in 2020 estimated the number of people living with HIV at 543,100, with 29,557 new infections and 30,137 deaths. The number of reported HIV-positive cases tends to increase year after year. The majority of HIV and AIDS cases are found in the productive age group 15-49 (Ministry of Health, 2022). HIV cascade data in 2022 shows that approximately 81% of people in Indonesia know their HIV status, 42% of whom are receiving treatment, and only 19% are virally suppressed. Therefore, the government's commitment through the Ministry of Health is to develop a strategy for combating HIV, AIDS, and STIs that refers to the Global Strategy with a fast track and targets the achievement of the "90-90-90" target by 2027. This target was updated in 2021 to "95-95-95" in 2027. The 95-95-95 target includes: 95% of PLHIV know their HIV status, 95% of PLHIV who are HIV-inspired continue to receive ARV therapy, and 95% of PLHIV who receive ARV therapy experience viral suppression[3]

Bogor City is a region in West Java Province, geographically located in the center of Bogor Regency and close to the nation's capital, making it a strategically important center for economic growth and development, as well as other social activities. This potential contributes to high levels of community mobility, creating opportunities for the development of social problems, including health issues, including infectious diseases. The persistently high HIV incidence in Bogor City made it the second-highest HIV-positive region in West Java Province in 2020 and the fourth-highest in 2021. It is also one of the top five contributors to HIV cases in Indonesia.An evaluation of the HIV surveillance system implemented in Bogor City in 2021 revealed several HIV surveillance performance indicators that had not yet been achieved, including the percentage of people living with HIV (PLWHA) undergoing ARV treatment at only 27.7% and the percentage of people living with HIV

experiencing viral suppression (viral load <1000 copies/ml) at 57.3%. These conditions illustrate the persistently high rate of loss to follow-up in Bogor City.

In advanced HIV (AIDS) there is the potential for other infections known as opportunistic infections to enter. [4]Therefore, it is recommended to develop and implement effective interventions to support patients in achieving viral suppression among all people with HIV. [5]*Comparative qualitative analysis* studies also state that people who do not experience viral suppression are identified in those who have more delays in starting ART and more deviations in adherence . The conditions that occur caused by lack of acceptance of HIV status , stigma and economic difficulties. ([6]The implications of non-compliance with ARV treatment which can also affect the failure to achieve viral suppression due to ARV resistance have been proven from previous studies in Indonesia, Ukraine and Vietnam, namely people who have experienced resistance from the start experienced viral suppression compared to those who did not have resistance at the start (OR: 0.2; 95% CI: 0.05, 0.87; p = 0.032). In the intervention group, participants with baseline resistance were compared with participants without baseline resistance (OR: 0.17; 95% CI: 0.04, 0.79; p = 0.024), and Indonesia had a higher proportion of resistance than Ukraine and Vietnam, namely 24.1% (Palumbo et al., 2019). The development of antiretroviral drugs to treat HIV has transformed an almost always fatal infection into a manageable chronic condition. Daily antiretroviral therapy can reduce the amount of HIV in the blood to levels undetectable by standard tests. Continuing treatment is very important to keep the virus suppressed[6].

NIAID-supported research has shown that achieving and maintaining a high viral load over a long period not only maintains the health of people living with HIV but also prevents sexual transmission of the virus to HIV-positive partners. HIV risk factor control aims to change the behavior of individuals or groups to break the chain of transmission or prevent disease, by changing risky behaviors for HIV infection to non-risky behaviors; and by changing community behaviors regarding accessing accurate information and seeking HIV treatment. ARV therapy adherence is one example of behavioral risk factor control. Adherence to ART can be influenced by a number of factors, including the patient's social and clinical situation, the prescribed regimen, and the patient-provider relationship. Poor adherence is often a consequence of one or more behavioral, structural, and psychosocial barriers (depression and other mental illnesses, neurocognitive disorders, low health literacy, low levels of social support, stressful life events including trauma, busy or unstructured daily routines, substance use, homelessness, poverty, non-disclosure of HIV serostatus, denial, and stigma). , inconsistent access to medication due to financial and insurance status [7]

Adherence to ARV treatment is essential for people living with HIV (PLWHA) to achieve successful treatment. Conversely, non-adherence can lead to virological failure. Virological failure is an early sign of treatment failure. Over time, virological failure is followed by immunological failure and ultimately clinical failure. This condition is usually characterized by the recurrence of opportunistic infections. Viral load testing is performed to detect treatment failure earlier and more accurately than monitoring using immunological or clinical criteria. This effort can prevent increased morbidity and mortality in people living with HIV. [8] Therefore, this study focuses on the influence of adherence on the risk of virological failure, as measured by the achievement of viral suppression, in people living with HIV in Bogor City.

MATERIAL DAN METHOD

This research is a quantitative study using an analytical observational method with *a case-control study design* . This design is used to examine the relationship between the effects of health problems and certain risk factors . This study design was chosen because it is technically easier and less expensive than other analytical designs. The low number of cases of viral suppression in people with HIV and the long incubation period of HIV infection were also considerations in the design selection. The causal relationship between a case-control design and a cross-sectional design is stronger.[9]This study examines the relationship between ARV adherence and viral suppression in people with HIV in Bogor City by comparing case and control groups based on their adherence status . This study can be used to determine whether the case and control groups have different proportions of those who have been exposed to the risk factors studied. PLHIV cases were recorded as not suppressed according to the results of the VL examination while PLHIV controls were recorded as suppressed according to the results of the VL examination, with inclusion criteria Age ≥18 years at the time of the start of ARV treatment incomplete exclusion criteria PLHIV not suppressed who met the inclusion and exclusion criteria. The secondary data in this study is the data from the HIV/AIDS and STI information system version 1.6 of Bogor City. This research design was chosen because it is technically easier and cheaper than other analytical designs. The number of cases of viral suppression in people with HIV is still low and the long incubation period of HIV infection is also a consideration in selecting the design. Population All people with HIV undergoing ARV treatment who have had their viral load checked in Bogor City until May 2023. The total population is 949, consisting of the case population Cases (N=84) of PLHIV recorded as not suppressed according to VL examination results and control population Control (N= 252) **.** PLHIV recorded as suppressed according to VL examination results Number of samples The sample in this study is a representative part of the study population. The case group is people with HIV in Bogor City who have

received ARV treatment with virological examination (viral load ≥1000 copies/ml) and reported as not suppressed in the HIV AIDS and STI information system data (SIHA version 1.7).

The control group is people with HIV in Bogor City who received ARV treatment and with virological examination (viral load <1000 copies/ml) and reported as suppressed in the HIV AIDS and STI information system data (SIHA version 1.7). The analysis was conducted descriptively to obtain a frequency distribution of the collected data, including independent and dependent variables, as well as covariate data for cases and controls. The results of the analysis included a frequency distribution of each of the variables studied: adherence to antiretroviral therapy, virology, age, gender, education, occupation, marital status, injecting drug users, men who have sex with men, clinical stage, duration of ART, ARV regimen, and opportunistic infections. Stratification analysis was conducted to determine whether age, gender, education, occupation, marital status, injecting drug users, men who have sex with men, clinical stage, duration of ART, ARV regimen, and opportunistic infections were confounding variables in the relationship between ARV adherence and viral suppression. Therefore, each variable's relationship between ARV adherence and viral suppression in people with HIV was stratified based on the respective covariate variables to calculate the crude OR and adjusted OR for each variable. If the difference between the crude OR and the adjusted OR was greater than 10%, then the variable was considered a confounding variable that must be controlled for in the multivariate analysis. Furthermore, to determine the differences in the effect of adherence on viral suppression based on ART duration, opportunistic infections, and nutritional status, a homogeneity test was performed to assess effect modification. If the p-value from the test of homogeneity was <0.05, indicating heterogeneity, it means that the variable statistically modifies the relationship between adherence and viral suppression. Conversely, if the p-value from the test of homogeneity was >0.05, indicating homogeneity, it means that the variable statistically modifies the relationship between adherence and viral suppression. Multifariat analysis uses a causal model with a backward predictor variable selection method, where all potential confounder variables are entered into the model first (full model), then their respective ORs are examined. Evaluation is performed by excluding the smallest association (OR) to determine whether the variable interferes with the relationship between the primary exposure and the outcome. The results of the multivariate analysis will be reported as odds ratios and 95% confidence intervals.

RESULT

The population of this study were patients with HIV who had been tested for viral load in Bogor City at 11 health facilities providing PDP services in Bogor City including Marzoeki Mahdi Hospital, Medika Dramaga Hospital, Indonesian Red Cross Hospital, Central Bogor Community Health Center, East Bogor Community Health Center, South Bogor Community Health Center, Sempur Community Health Center, Sindang Barang Community Health Center, Tanah Sareal Community Health Center, Kedung Badak Community Health Center, and Warung Jambu Community Health Center. Data were taken from viral load examinations carried out until May 2023, totaling 943 with 98 cases and 851 controls. Sample selection was carried out through data review and observation by considering the inclusion criteria, namely PLHIV aged ≥ 18 years and exclusion criteria, namely incomplete PLHIV data and viral load examinations under 6 months, so that the final sample was 84 cases and 3 times larger than the number of cases, namely 252 controls.

Descriptive Analysis Results

Descriptive analysis was carried out to determine the frequency distribution of each variable studied, which can be seen in the following table.

Table 1. Characteristics of People with HIV in Bogor City

Variables	Case		Control		Total	
	n	%	n	%	n	%
Compliance						
Low	29	34.52	13	5.16	42	12.50
Tall	55	65.48	239	94.84	294	87.50
Age						
<40 Years	73	86.90	214	84.92	287	85.42
≥40 Years	11	13.10	38	15.08	49	15.48
Gender						
Man	63	75.00	186	73.41	248	73.81
Woman	21	25.00	67	26.59	88	26.19
Education						
Low	13	15.48	39	15.48	52	15.48
Tall	71	84.52	213	84.52	284	84.52

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Variables	Case		Control		Total	
	n	%	n	%	n	%
Work						
Work	58	69.05	179	71.03	237	70.54
Doesn't work	26	30.95	73	28.97	99	29.46
Marriage						
Not married yet	64	76.19	156	61.90	220	65.48
Marry	20	23.81	96	38.10	116	34.52
Male Sex Male						
Yes	44	52.38	149	59.13	193	57.44
No	40	47.62	103	40.87	143	42.56
Drug addicts						
Yes	15	17.86	21	8.33	36	10.71
No	69	82.14	231	91.67	300	89.29
Clinical Stage						
Stage 3 & 4	37	44.05	123	48.81	160	47.62
Stage 1 & 2	47	55.95	129	51.19	176	52.38
Duration of ART						
≤12 Months	5	5.95	34	13.49	39	11.61
>12 Months	79	94.05	214	86.51	297	88.39
Opportunistic infections						
Yes	15	17.86	59	23.41	74	22.02
No	69	82.14	143	76.59	262	77.98
Regimen						
Line 2	15	17.86	13	5.16	28	8.33
Line 1	69	82.14	239	94.84	308	91.67

The table above shows the results of the study on people with HIV with low adherence, which was more common in the case group, as many as 29 people (34.52%) compared to the control group, as many as 13 people (5.16%). People with HIV with high adherence were also more common in the control group, as many as 239 people (94.84%) and in the case group, as many as 55 people (65.48). Grouping by age, people with HIV aged <40 years were more common in the case group, as many as 214 (84.92) compared to the case group, as many as 73 people (86.90). People with HIV aged ≥40 were more common in the control group, as many as 38 people (15.08) and the case group, as many as 11 people (13.10). Meanwhile, based on gender, people with HIV in Bogor City are mostly male with a proportion of 73.81% in the case group of 63 people (75%) and the control group of 86 (73.41%), and the female gender is also more numerous in the control group of 67 people (26.59%) and the case group of 21 people (25%).

The results of the analysis also show that in general HIV cases in Bogor City are in those with a high level of education with a proportion of 84.52% and more in the control group, namely 213 people (84.52%) and the case group as many as 71 (84.52%), with the same comparison also occurring in cases of people with HIV with low levels of education. The results of the analysis can also be seen based on employment status where people with HIV who work in the case group are 58 people (69.05) and the control group as many as 179 people (71.03), while in those who do not work in the case group as many as 26 (30.95%) and the control group as many as 73 people (28.97%). Based on the marital status of people with HIV who are not married in the case group as many as 64 people (76.19%) and the control group as many as 156 people (61.90%), while those who are married in the case group as many as 20 people (23.81%) and the control group as many as 96 people (38.10%). The table above also shows an analysis based on behavioral factors where men who have sex with men are more in the control group, namely 149 people (59.13%) compared to the case group as many as 44 people (52.38%) and those who are not classified as men who have sex with men are also more in the control group than the case group. While injecting drug users are also more in the control group, namely 231 people (91.67%) compared to the case group as many as 44% (52.38%). Grouping based on clinical conditions of people with HIV based on severe clinical symptoms, namely stage 3 and stage 4, was more in the control group, namely 123 people (48.81%) and the case group as many as 44.05, as well as based on mild symptoms and or asymptomatic, namely stage 1 and stage 2, was also more in the control group as many as 129 people (51.19) and the case group as many as 47 people (55.95%). Based on the duration of treatment ≤12 months in the case group as many as 5 people (5.95%) and the control group as many as 34 people (13.49%), while the duration of treatment >12 months in the case group as many as 79 people (94.05%) and the group 214 people (86.51%). Based on the presence of opportunistic

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infections in the case group as many as 15 people (17.86) and in the control group as many as 59 people (23.41%), while those who did not experience opportunistic infections during treatment in the case group as many as 69 people (82.14%) and the control group as many as 143 people (76.59%). Based on the regimen used in treatment, namely the second-line regimen in the case group as many as 15 people (17.86%) and the control group as many as 13 people (5.16%), while the use of the first-line regimen in the case group as many as 69 people (82.14%) and in the control group as many as 239 (94.84%).

Stratification Analysis Results

Stratification analysis was conducted before multivariate analysis to determine the extent of the influence of covariate variables on the relationship between adherence levels and viral suppression in people with HIV by observing the magnitude of the risk difference before and after being controlled with covariate variables and also observing whether there is a modification effect of the relationship. The presence of a modification effect can be seen from the p-value (Pr>chi2) of the Test of Homogeneity results , if the p-value ≤ 0.05, then there is a significant difference in the OR value of each stratum, which means there is a modification effect. Conversely, if the p-value > 0.05, then there is no significant difference in the OR value in each stratum, meaning there is no modification effect. The results of the analysis are presented in the following table.

Table 2. Stratification Analysis of the Influence of Individual Characteristics On the Relationship of Compliance to Viral Suppression in People with HIV

Variables	Compliance	Case	Control	Total	OR crude (95%CI)	OR adjusted (95%CI)	ΔOR
Age							
<40 Years	Low	24	9	33	9.69	10.17	4.7
	Tall	94	205	299	(4.50-21.52)	(4.90-21.10)	
≥40 Years	Low	5	4	9			
	Tall	6	34	40			
Test of homogeneity, P-value: 0.6166							
Gender							
Man	Low	17	10	27	9.69	9.59	1
	Tall	46	175	225	(4.50-21.52)	(4.71-19.51)	
Woman	Low	12	3	15			
	Tall	9	64	73			
Test of homogeneity, P-value: 0.0828							
Education							
Low	Low	7	3	10	9.69	9.93	2.4
	Tall	6	36	42	(4.50-21.52)	(4.82-20.45)	
Tall	Low	22	10	32			
	Tall	49	203	252			
Test of homogeneity, P-value: 0.6398							
Work							
Work	Low	16	12	28	9.69	9.18	5.6
	Tall	42	167	209	(4.50-21.52)	(4.54-18.58)	
Doesn't work	Low	13	1	14			
	Tall	13	72	85			
Test of homogeneity, P-value: 0.0207							
Marriage							
Yes	Low	16	7	23	9.69	11.07	12
	Tall	48	149	197	(4.50-21.52)	(5.24-23.41)	
No	Low	13	6	19			
	Tall	7	90	97			
Test of homogeneity, P-value: 0.0837							

The results of the stratification analysis seen from the individual factors in the table above show that age is not a confounder with a change in OR of 4.7% (<10%) and a p-value from the results of the Test of Homogeneity of 0.6166, meaning that age does not provide a modifying effect on the relationship between adherence to antiretroviral therapy and viral suppression. This means that statistically there is no difference in risk based on age in people who are not virally suppressed. Based on the gender variable, it can also be seen that gender is not

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a confounder but is a confounder with a change in OR of 1% (<10%) and a p-value from the results of the Test of Homogeneity of 0.0828, meaning that gender does not provide a modifying effect on the relationship between adherence to antiretroviral therapy and viral suppression. This means that statistically there is no difference in the risk of viral unsuppression in men and women.

Based on the education variable, it can also be seen that education is not a confounder with a change in OR of 2.4 (<10%) and a p-value from the results of the Test of Homogeneity of 0.6398, meaning that education does not provide a modifying effect on the relationship between adherence to antiretroviral therapy and viral suppression. This means that statistically there is no difference in the risk of viral unsuppression in people with HIV with high or low education levels. Based on the employment variable, it can also be seen that employment is not a confounder with a change in OR of 5.4 (<10%) and a p-value from the results of the Test of Homogeneity of 0.0207, meaning that employment status modifies the relationship between adherence to antiretroviral therapy and viral suppression. This means that statistically there is a difference in the risk of viral unsuppression in people with HIV in people with HIV who are employed and those who are not employed. Based on the marital status variable, it can also be seen that marital status is a confounder with an OR change of 12 (>10%) and a p-value from the homogeneity test of 0.0837, meaning that marital status does not modify the relationship between antiretroviral therapy adherence and viral suppression. This means that statistically there is no difference in the risk of viral suppression in married and unmarried people with HIV

Table 3. Stratification Analysis of the Influence of Individual Behavior On the Relationship of Compliance to Viral Suppression in People with HIV

Variables	Compliance	Case	Control	Total	OR $_{crude}$ (95%CI)	OR $_{adjusted}$ (95%CI)	ΔOR
Drug addicts							
Yes	Low	4	4	8	9.69	8.02	20.8
	Tall	11	17	28	(4.50-21.52)	(3.91-16.41)	
No	Low	25	9	34			
	Tall	4	222	226			
Test of homogeneity, P-value: 0.0150							
MSM							
Yes	Low	10	6	16	9.69	9.67	0.2
	Tall	34	143	177	(4.50-21.52)	(4.70-19.92)	
No	Low	9	7	16			
	Tall	21	96	117			
Test of homogeneity, P-value: 0.4437							

The stratification analysis of behavioral influences in the table above shows that injecting drug users in people with HIV have the potential to be confounding in the relationship between antiretroviral therapy adherence and viral suppression, as seen from the change in OR (ΔOR) of 20.8% (>10%). The p-value obtained from the homogeneity test is 0.0150 (<0.05), so it is stated that injecting drug use behavior modifies the relationship between antiretroviral therapy adherence and viral suppression in people with HIV in Bogor City. Meanwhile, sexual behavior (men having sex with men) does not have the potential to be confounding because the change in OR (ΔOR) is 0.2% (<10%), with a p-value obtained from the homogeneity test of 0.4437 (>0.05), meaning that the male sex with men factor does not modify the relationship between adherence and viral suppression in people with HIV in Bogor City.

Table 4. Influence of Clinical Factors on the Relationship between Compliance e and On Viral Suppression in People With HIV

Variables	Compliance	Case	Control	Total	OR $_{crude}$ (95%CI)	OR $_{adjusted}$ (95%CI)	ΔOR
Clinical Stage							
Stage 1&2	Low	17	6	23	9.69	9.69	0
	Tall	20	117	137	(4.50-21.52)	(4.74-19.80)	
Stage 3&4	Low	12	7	19			
	Tall	35	122	157			
Test of homogeneity, P-value: 0.1677							
Duration of ART							
≤12 Months	Low	3	1	4	9.69	9.38	2.3

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Variables	Compliance	Case	Control	Total	OR crude (95%CI)	OR adjusted (95%CI)	ΔOR
	Tall	2	33	35	(4.50-21.52)	(4.58-19.20)	
>12 Months	Low	56	12	68			
	Tall	23	206	229			
Test of homogeneity, P-value: 0.2110							
Opportunistic Infections							
	Low	6	2	8	9.69	9.47	2.3
Yes	Tall	9	57	66	(4.50-21.52)	(4.63-19.37)	
	Low	23	11	34			
No	Tall	46	182	228			
Test of homogeneity, P-value: 0.3953							
Regimen							
Line 2	Low	5	1	6	9.69	9.40	3.1
	Tall	10	12	22	(4.50-21.52)	(4.50-19.62)	
Line 1	Low	25	12	37			
	Tall	45	227	272			
Test of homogeneity, P-value: 0.6724							

The results of the stratification analysis of the influence of clinical factors indicate that clinical stage, duration of treatment, opportunistic infections, and regimen are not potential confounding factors in the relationship between adherence and viral suppression in people with HIV, as seen from the change in OR (ΔOR) of >10%. The stratification analysis shows that clinical stage, duration of treatment, opportunistic infections, and regimen do not modify the relationship between adherence and viral suppression in people with HIV in Bogor City. The results of the stratification analysis of each variable are summarized in the following table. Based on the stratification analysis of all variables, it can be seen that the variables of marriage and injecting drug users are potential confounding factors in the relationship between adherence and viral suppression because ΔHR >10%. Therefore, these variables will be included again in the multivariate analysis to ensure the actual confounding . In addition, the stratification analysis above also shows that only the variables of injecting drug users and employment status provide a modification effect (interaction) on the relationship between adherence and viral suppression in people with HIV because the p-value of the test of homogeneity <0.05.

Multivariate Analysis Results

This study aimed to determine the relationship between adherence and viral suppression after controlling for covariates such as age, gender, education, occupation, marriage, injection drug use, clinical stage, duration of treatment, opportunistic infections, and regimen using logistic regression analysis. The results of the multivariate analysis are presented in each step of the analysis below.

Full Model

Multivariate analysis at this stage uses logistic regression analysis, which is the initial step of multivariate analysis aimed at determining the estimated odds ratio of adherence to viral suppression after controlling for covariate variables, namely age, gender, education level, occupation, marital status, injecting drug users, men who have sex with men, clinical stage, duration of treatment, opportunistic infections, and treatment regimen. This analysis consists of identifying interaction variables and confounder variables, which then produce a final model that will be interpreted as the final result of the association of adherence with viral suppression in people with HIV. Initial multivariate modeling begins by entering the main independent variables and all covariate variables. The following table presents the results of the full multivariate analysis model of the relationship between adherence to antiretroviral therapy and viral suppression in people with HIV in Bogor City.

Table 6. Full Model Multivariate Analysis of Compliance Relationships With Viral Suppression in People With HIV

Variables	OR	95% CI	P-value
Compliance	**14.04**	6.02 - 32.74	0.000
Age	0.87	0.34 - 2.20	0.768
Gender	1.43	0.57 - 3.56	0.442
Education	0.56	0.23 - 1.34	0.190
Work	0.69	0.33 - 1.40	0.302

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Variables	OR	95% CI	P-value
Marriage	5.06	2.13 - 12.01	0.000
Drug	2.58	1.06 - 6.33	0.038
Male Sex Male	0.48	0.21 - 1.11	0.087
Clinical Stage	0.58	0.30 - 1.13	0.107
Duration of ART	0.50	0.15 - 1.34	0.152
Opportunistic Infections	0.95	0.42 - 2.14	0.900
Regimen	5.16	1.98 - 13.40	0.001

Based on the table above, it can be seen that the association of ARV therapy adherence with viral suppression before being controlled with confounder variables is 14.04 (95% CI: 6.02 - 32.74).

Confounding Test

Confounding analysis is conducted to identify covariate variables that act as confounders in the relationship between the main independent variable and the dependent variable. This is done by gradually removing the variable with the smallest OR value. The following are the stages of the confounding test in multivariate analysis.

Table 7. Multivariate Logistic Regression Modeling Confounding Test
The Relationship Between ARV Therapy Compliance and Viral Suppression in People with HIV

Stage	OR	P-value	ΔOR	Information
Full Model				All covariate variables are included in the model.
Compliance	14.04		-	
Stage 1				
Compliance	13.81	0.000		
Age	0.86	0.748		
Gender	0.94	0.882		
Education	0.64	0.306		
Work	0.66	0.247		Releasing LSL
Marriage	4.01	0.001	1.67	Not a Confounder
Drug addicts	3.07	0.012		
Clinical Stage	0.64	0.173		
Duration of ART	0.45	0.155		
Opportunistic Infections	0.97	0.936		
Regimen	5.41	0.000		
Stage 2				
Compliance	13.49	0.000		
Age	0.88	0.777		
Gender	0.90	0.799		
Education	0.64	0.310		
Work	0.71	0.337		Issuing ART Duration
Marriage	4.09	0.001	4.08	Not a Confounder
Drug addicts	3.37	0.006		
Clinical Stage	0.65	0.189		
Opportunistic Infections	0.95	0.909		
Regimen	5.69	0.000		
Stage 3				
Compliance	12.76	0.000	10.03	
Age	0.88	0.793		
Gender	0.88	0.751		Issuing Education
Work	0.79	0.485		Change in OR >10%
Marriage	3.96	0.001		Confounder
Drug addicts	3.37	0.006		
Clinical Stage	0.63	0.164		
Opportunistic Infections	0.94	0.870		
Regimen	5.64	0.000		
Stage 4				Removing Clinical Stage

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Stage	OR	P-value	ΔOR	Information
Compliance	12.74	0.000	10.20	Change in OR >10% Confounder
Age	0.90	0.816		
Gender	0.85	0.679		
Education	0.62	0.268		
Work	0.72	0.366		
Marriage	4.10	0.001		
Drug addicts	3.35	0.006		
Opportunistic Infections	0.78	0.507		
Regimen	5.14	0.001		
Stage 5				
Compliance	13.18	0.000	6.52	Issue Jobs Change in OR <10% Not a Confounder
Age	0.89	0.797		
Gender	0.79	0.520		
Education	0.72	0.431		
Marriage	4.07	0.001		
Drug addicts	3.32	0.006		
Clinical Stage	0.66	0.202		
Opportunistic Infections	0.94	0.886		
Regimen	5.52	0.000		
Stage 6				
Compliance	13.22	0.000	6.20	Removing Age Change in OR <10% Not a Confounder
Gender	0.79	0.528		
Education	0.72	0.433		
Marriage	3.91	0.000		
Drug addicts	3.33	0.006		
Clinical Stage	0.66	0.206		
Opportunistic Infections	0.94	0.879		
Regimen	5.53	0.000		
Stage 7				
Compliance	13.28	0.000	5.72	Eliminating Opportunistic Infections Change in OR <10% Not a Confounder
Gender	0.80	0.540		
Education	0.72	0.429		
Marriage	3.92	0.000		
Drug addicts	3.35	0.006		
Clinical Stage	0.65	0.153		
Regimen	5.50	0.000		
Stage 8				
Compliance	13.53	0.000	3.77	Revealing Gender Change in OR <10% Not a Confounder
Education	0.73	0.445		
Marriage	3.70	0.000		
Drug addicts	3.29	0.007		
Clinical Stage	0.64	0.146		
Regimen	5.31	0.000		
Stage 9				
Compliance	13.82	0.000	1.5	Expelling Drug Users Change in OR <10% Not a Confounder
Education	0.72	0.427		
Marriage	3.00	0.002		
Clinical Stage	0.64	0.136		
Regimen	4.86	0.001		
Stage 10				
Compliance	10:55	0.000	33	Issuing Marriage Change in OR >10% Confounder
Education	0.80	0.573		
Clinical Stage	0.61	0.089		
Regimen	4.60	0.001		
Stage 11				
Compliance	13.39	0.000	4.85	Issuing Regimen Change in OR >10% Not a Confounder
Education	0.74	0.450		

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Stage	OR	P-value	ΔOR	Information
Marriage	2.88	0.002		
Clinical Stage	0.77	0.363		

the confounding analysis in the table above indicate that the covariate variables acting as confounders with a change in OR (**ΔOR**) of >10% in the relationship between antiretroviral therapy adherence and viral suppression in people with HIV in Bogor City are education, marital status, and clinical stage. These confounder variables will be controlled for and their influence will be assessed in the final model.

Final Model

The final model describes the relationship between antiretroviral therapy adherence and viral suppression in people with HIV after controlling for confounder variables such as education, marital status, and clinical stage. The final modeling can be seen in the following table.

Table 8. Final Model of Multivariate Logistic Regression Analysis of the Relationship between Antiretroviral Therapy Compliance and Viral Suppression in People with HIV in Bogor City

Variables	β	OR (95% CI)	P-value
Compliance	2,594	13.39 (6.09 - 29.41)	0.000
Education	-0.30 3	0.74 (0.34 - 1.62)	0.450
Marriage	1,056	2.88 (1.48 - 5.59)	0.002
Clinical Stage	-0.259	0.77 (0.44 - 1.35)	0.363

The final modeling results of multivariate analysis using logistic regression obtained an OR value for the relationship between the level of antiretroviral adherence and viral suppression in people with HIV in Bogor City of 13.39 (95% CI 6.09 - 29.41), meaning that people with HIV in Bogor City with low adherence have a 13.39 times greater risk of viral non-suppression compared to people with HIV with high adherence to antiretroviral therapy after being controlled for variables of education, marital status and clinical stage.

DISCUSSION

HIV remains a major global public health issue, particularly in Indonesia, which has the highest HIV infection rate in Southeast Asia. [10]HIV is also a disease with the highest threat of emerging diseases, with the highest prevalence among those aged 20-49, who are essential human resources for national development. Therefore, addressing HIV is a priority and requires special attention, including comprehensive prevention and control measures, addressing influencing risk factors. One of these is treatment retention, which is related to adherence and viral suppression in people living with HIV, which is one of the goals of global HIV control. Research related to HIV issues is still very limited in Indonesia, especially regarding virological failure. Meanwhile, other studies have focused only on immunological failure and clinical failure related to HIV issues. Therefore, this study was conducted to serve as a reference for implementing control measures in HIV programs, particularly those related to the increase in people with HIV experiencing viral suppression, namely achieving <1000 copies/ml of blood during viral load testing during ARV treatment, which is one of the targets that must be achieved in controlling HIV issues and improving programs and services.

The Relationship between Antiretroviral Therapy Adherence and Viral Suppression

The clinical efficacy of antiretroviral therapy (ART) in suppressing HIV and improving survival in people with HIV has been proven. To achieve optimal results from ARV therapy, a high level of adherence to ARV therapy in HIV patients is crucial. Long-term HIV treatment with adherence of more than 95% can reduce the increase in viral load and improve the immune system. Conversely, non-adherence can cause treatment failure and accelerate the occurrence of HIV drug resistance, as well as the development of AIDS more quickly. Most people with low adherence to ARV therapy cannot achieve viral suppression.[11] The final model of the results of the multivariate analysis in the study showed a significant association between adherence to antiretroviral therapy and viral suppression in people with HIV in Bogor City with a magnitude of 13.39 (95% CI: 6.09 - 29.41, p-value: 0.000). This means that people with HIV in Bogor City with low adherence have a 13.39 times greater risk of viral suppression compared to people with HIV with high adherence to antiretroviral therapy after controlling for covariate variables.

Poor medication adherence is a risk factor for the emergence of drug-resistant HIV strains and can potentially infecting others . [12]Poor medication adherence not only endangers individual health but also increases transmission, makes treatment more difficult, and leads to more severe public health problems . [13]This study

identified risk factors that are effect modifiers, namely injection drug users and employment status. It was found that the proportion of injection needle users among people with HIV in Bogor City who did not experience viral suppression was greater than in people with suppressed HIV. Stratification analysis showed a difference in the risk of viral suppression in people with HIV between those who inject drugs and those who do not inject drugs with a p-value obtained from the homogeneity test of 0.0150 . A study suggested that people with HIV who inject drugs were found to be significantly less responsive to ARV therapy and viral suppression. Medication adherence is strongly associated with the use of illicit substances such as opiates and cocaine. The study found that PLWHA who use opioids showed significantly reduced ART adherence (63%), compared to non-drug users (79%) [14]. Drug-drug interactions due to the induction of metabolic enzymes or transporters, which can result in reduced subtherapeutic drug concentrations. This can lead to poorer antiretroviral therapy outcomes in people with HIV. Differences in relative susceptibility to metabolic enzymes and transporters can affect the absorption, distribution, metabolism, and excretion of antiretrovirals. Work plays an economic role in meeting family needs. People with HIV generally strive to earn money to meet family needs and cover medical expenses because they want to recover and live. High levels of work activity can lead to poor adherence to treatment, which ultimately leads to decreased viral suppression. In a study in Nigeria, it was found that work had a significant relationship with adherence to treatment with a high risk in each job, namely working in the government (OR: 2.842; p <0.01 and self-employed (OR: 2.6; p <0.001), this was associated with some people with HIV being those who had higher education with low ART adherence, this was in accordance with the fact that groups of people with HIV with high levels of education had jobs with many job desks making it difficult for them to take medication. Busy work schedules and forgetting to take medication were reasons for non-adherence in undergoing treatment [15]

In this study, several risk factors were also identified that act as confounders in the relationship between ARV therapy adherence and viral suppression, namely education level, marital status and clinical stage. In relation to the educational risk factor, this study showed that education is a confounder in the relationship between adherence to antiretroviral therapy and viral suppression in people with HIV in Bogor City with a risk of 0.74 (95% CI: 0.34 - 1.62). Higher education levels were higher in people with HIV in both the case and control groups compared to people with HIV with low education levels. This indicates that education provides a protective effect on the relationship where high education cannot make someone achieve viral suppression or in other words that low education does not make someone not achieve viral suppression but the opposite can also occur. The results of this study are in line with a cross-sectional survey research design study in Nigeria showing that adherence in people living with HIV and AIDS who have no education or pre-secondary education is significantly better than those with post-secondary education ($\chi 2$ = 23.448: P <0.05). This study showed that the proportion of patients with basic education who adhered to treatment was 88.3% compared to those with higher education levels, where only 67% adhered to treatment.([8]) Higher education generally has a positive influence on the ease of absorbing knowledge in the form of information provided during counseling, which results in changes in compliance behavior for the better. However, research A study in Yogyakarta also found similar results to this study, showing no significant relationship between knowledge level and adherence to ARV therapy in people living with HIV (p = 0.153; r = 0.113) [11]. Many other studies have also yielded results consistent with this study, using different research designs. People living with HIV with good knowledge do not necessarily have high adherence. Many other factors influence adherence to ARV therapy, not just knowledge level, including individual awareness and motivation, workload, medication side effects, and reluctance to take medication when it runs out.[12] Another risk factor found as a confounder in the relationship between ARV therapy adherence and viral suppression in people with HIV in Bogor City is marital status with a risk of 2.88 (95% CI: 1.48 - 5.59, p-value: 0.002).

Unmarried individuals living with HIV in Bogor City were found to have a higher proportion (76.19%) in the case group than in the control group (61.90%). The results of this study align with other findings in North American studies that marriage among heterosexuals significantly contributes to achieving a faster response to HIV treatment. The results showed that married individuals had a 69% higher rate of viral suppression, with a hazard ratio of 1.69 (95% CI: 1.02 - 2.78) compared to unmarried individuals.1 In other studies, adherence to ARV therapy was also influenced by family support. Increased adherence occurred in individuals living with HIV who had positive family support, with a proportion of 53.7% (p = 0.034). Adherence to ARV therapy can also be influenced by the internal motivation of PLWHA to recover and survive. Good motivation in PLWHA will influence optimism in life, enthusiasm for work, positive thinking, and adherence to ARV treatment.[7]. Other studies also show the same results that sociodemographic factors such as marital status, and other personal factors, namely support from friends and family members, are significantly associated with adherence to ART (OR: 1.586; CI: 1.097 -2.292) [16].

The results of this study also corroborate previous research, which found that social support significantly influences adherence; the greater the social support provided by family and sexual partners, the greater the likelihood of adherence to ARV medication. Families play a crucial role in improving, assisting, and encouraging patients to adhere to their treatment regimen[17]. Another finding in this study is that clinical stage can interfere with the relationship between ARV therapy adherence and viral suppression, with an association of 0.77 (95% CI: 0.44 - 1.35, p-value: 0.363). The descriptive analysis showed that the proportion of people with HIV in Bogor

City with severe clinical symptoms, namely stage 3 and stage 4, was higher in the control group (45.81%) compared to the control group (48.81%). Meanwhile, the proportion of people with HIV in Bogor City diagnosed with mild symptoms at the time of initial ART initiation was higher in the case group (55.95%) compared to the control group (51.19%). Previous research stated that patients diagnosed in stages II and III based on the WHO classification have a higher possibility of increasing viral load compared to patients diagnosed in stage I. This shows that patients in these stages have a decreased immune system due to opportunistic infections and comorbidities experienced, thus increasing the ability to increase [18] The above occurs because HIV patients diagnosed with severe symptoms are usually accompanied by opportunistic infections, so they require additional therapy in addition to the HIV regimen, which affects the level of compliance due to the complexity of the dose and regimen given.

The above research is in line with the results of other research by diethioupia which found people with HIV in good clinical condition with no opportunistic infections. (AHR = 1.84; 95% CI = 1.34, 2.52), high CD4 count at initial examination (AHR: 1.87; 95% CI = 1.34, 2.63) , diagnosed with stage I & II (AHR = 2.12; 95% CI = 1.18, 3.79), and received tuberculosis preventive therapy (AHR = 2.24; 95% CI = 1.66, 3.02) experienced faster viral suppression(Erjino et al., 2023). The results in this study were found to be different, with a risk of OR<1, and clinical stage as a confounder in the study had a protective effect on the relationship. This study is in line with research in Ethiopia, where there was no significant association between WHO clinical stage and adherence [19]levels . This can occur because people with HIV who present with asymptomatic or mild symptoms tend to neglect ARV therapy adherence because they feel fine and are in a manageable condition. This can lead to neglecting ARV therapy, leading to HIV progression and a lack of viral suppression. Furthermore, in the early stages of infection, people tend to seek solutions by trying alternative treatments, thus neglecting ARV therapy, the gold standard for suppressing HIV virus development. This poor adherence behavior can increase the likelihood of HIV drug resistance, which can compromise the effectiveness of antiretroviral drugs[20]. Other studies have found that patients with low socioeconomic status, low baseline viral loads, and higher baseline CD4 counts have consistently lower adherence than other patients across all regimens. A meta-analysis also found that patients who do not perceive their disease as severe or threatening are more than 1.5 times more likely to be non-adherent. A high baseline CD4 count indicates no deterioration,[23] indicating a patient's immune system is in excellent condition. This condition makes people with HIV feel that therapy is not yet important to continue . The importance of identifying risk factors that act as confounding factors in the relationship between ARV therapy adherence and viral suppression is to help identify barriers to adherence in the counseling process to address the problem appropriately so that problems related to non-adherence can be corrected and the achievement of viral suppression in people with HIV can be increased.[25]

CONCLUSION AND SUGGESTIONS

The conclusion of the study on the relationship between adherence to antiretroviral therapy and viral suppression in people with HIV in Bogor City is that people with HIV in Bogor City who do not experience viral suppression have a low level of adherence with a proportion of 34.52% greater than the group of people with HIV who experience viral suppression with a proportion of only 5.16% at the same level of adherence. The identified risk factors that act as known effect modifiers from the homogeneity test of stratification analysis are injection drug users (p=0.0150) and employment status (p=0.0207). Potential confounding risk factors in the relationship between antiretroviral therapy adherence and viral suppression in people with HIV in Bogor City are education level (OR: 0.74; 95% CI: 0.34 - 1.62), marital status (OR: 2.88; 95% CI: 1.48 - 5.59), and clinical stage (OR: 0.77; 95% CI: 0.44 - 1.35). HIV sufferers in Bogor City with low adherence have a 13.39 times risk (95% CI 6.09 - 29.41) of viral suppression compared to people with HIV with high adherence to antiretroviral therapy after controlling for potential confounding variables, namely education, health, and clinical stage. It is recommended to conduct studies on drug resistance in people with HIV in relation to viral suppression.

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