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A Double Burden: Evaluating Chronic Obstructive Pulmonary Disease in People Living with HIV Attending an ART Clinic in Addis Ababa

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Abstract **Background:** While HIV patients live longer, they can develop non-HIV-related health issues. Chronic obstructive pulmonary disease (COPD) is a concern, but data on COPD in HIV patients in Ethiopia is limited. **Objective:** This study assessed the prevalence and factors associated with COPD among people living with HIV(PLWH) attending the anti-retroviral therapy (ART) clinic at Tikur Anbesa Specialized Hospital in Addis Ababa, Ethiopia. **Methods:** Participants underwent screening for COPD using a structured questionnaire that assessed sociodemographic, clinical, and HIV/AIDS-related information. Postbronchodilator spirometry was performed with COPD defined per the Global Initiative for Obstructive Lung Disease (GOLD) criteria (FEV1/FVC) ratio < 0.7. The data was analyzed using SPSS version 26, and factors related to COPD were explored using logistic regression models. **Results:** Most participants were female (69%) and urban residents (99%). While smoking prevalence was low (9.9%), 66.7% reported exposure to biomass fuel. Chronic respiratory symptoms were common (dyspnea: 39.9%, chronic cough: 22.5%, phlegm: 14.1%, wheezing: 4.2%). COPD prevalence was 4.7% (10/213). Self-reported chronic cough (AOR=4.4, p=0.045) and smoking history (AOR=8.5, p=0.031) were associated with COPD. **Conclusion:** This study found a high burden of respiratory symptoms but a low prevalence of COPD in PLWH on ART. Chronic cough and smoking were associated with COPD in PLWH.

Keywords: *HIV, COPD, spirometry, Smoking*

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1. Introduction

HIV continues to be a significant public health issue. Approximately 38.4 million people were living with HIV by the end of 2021. It is estimated that 0.7% of the world's population between the ages of 15 and 49 have HIV; however, the severity of the epidemic differs across countries and regions [1]. According to a World Health Organization (WHO) report, Africa remains the most severely impacted region of the world, with one out of every twenty-five individuals (3.4%) living with HIV, representing more than two-thirds of all HIV patients worldwide. By 2021, there were more than 1.5 million additional infections and 650,000 deaths due to the disease, with 60% of the new infections arising in sub-Saharan Africa [2].

PLWH lives longer due to widespread access to efficient antiretroviral medication (ART) [3,4]. Non-communicable diseases (NCDs) are increasingly displacing advanced HIV as a significant cause of morbidity and mortality in HIV-infected people in many regions of the world. The overall aging of the HIV population [5,6] Underlines this trend.

Chronic obstructive pulmonary disease (COPD), a significant NCD in the HIV population, ranks third among the most common causes of death globally, accounting for 6% of all deaths in 2020 [7,8]. Therefore, it is imperative for clinicians working with PLWH to have a thorough understanding of the prevalence, diagnosis, and treatment of COPD.

Numerous epidemiological studies have shown that PLWH has a greater frequency of COPD. Studies conducted over 20 years, primarily in North America and Europe, revealed a prevalence of COPD ranging from 3.4% to over 40% [9]. The vast differences in these studies may be mainly attributable to variations in smoking prevalence, age at study entry, and other characteristics in these cohorts. Obstructive airway disease was the cause of approximately 4% of PLWH's fatalities in 1998, a threefold increase from the time before ART [10]. Since the early 1990s, there have also been more hospitalizations for COPD [11].

These findings, along with those from other long-term studies[12,13], imply that the rate at which PLWH show a decrease in their FEV1 and experience worsening airflow obstruction is higher than that of non-infected individuals. As PLWH continues to live longer, COPD may soon become a significant HIV comorbidity [13].

2. Methods

study design

A cross-sectional study was carried out to determine the prevalence of COPD and related factors among PLWH who were followed up at the ART clinic of Tikur Anbessa Specialized Hospital, the largest tertiary referral hospital in Addis Ababa, Ethiopia, from October 15 to December 2023. PLWHs aged ≥18 years who provided verbal informed consent and were free from acute illness were included in the study. Patients were excluded from the study if they had a contraindication to spirometry (e.g., acute cardiac/respiratory illness, active pulmonary TB, or pregnancy) or had declined to consent to participate in the study.

Sampling procedure

The first patient who visited the clinic on the first day of the study period was recruited. After that, a systematic random sampling method was used, assuming that 600–800 (average 700) patients are seen each month at the ART; = 700/220 = 3, so from all patients seen at the ART clinic, every 3rd patient was recruited into the study. Participants' medical records were documented to avoid redundancy.

Sample size determination

The sample size determination was based on a single population proportion formula. A prevalence of 15.4% was reported in a study performed in Nigeria in a similar population [1].

The sample size was calculated by assuming a confidence interval of 95%, a 5% margin of error, and a 10% nonresponse rate.

$$n = \frac{Z^2 x(p)(1-p)}{d^2}$$

Z-z score -1.96

d - margin of error- 0.05p - population proportion-15.4% (0.154)

n - Sample size- 200.19 ≈ 200

The weight and height of each participant were obtained using a stadiometer with a weighing scale, after which spirometry was carried out by a trained technician using an EASY ONE desktop spirometer by the protocol developed by the European Respiratory Society and American Thoracic Society (ERS/ATS) [14]. The highest value of the FEV1 and FVC out of three acceptable and reproducible readings for each participant was taken as the representative reading. All subjects with a postbronchodilator FEV1/FVC ratio < 0.7 were considered to have COPD and were included in this analysis. Reversibility was considered significant when the FEV1 increased by 200 ml and 12% from baseline. The spirometer was set to generate reports automatically based on the ATS/ERS 2021. Irrespective of automated reports, the primary investigator verified each spirometry reading for acceptability and consistency using the ERS/ATS criteria [14].

Statistical Analysis

Based on a COPD prevalence rate of 15.4% from a similar study performed in Nigeria [1], the sample size was determined after assuming a confidence interval of 95%, a -5% margin of error, and a 10% nonresponse rate, resulting in the required sample size of 220 participants. The data collected were checked for completeness and internal consistency by cross-checking. Subsequently, the data were entered and managed using the Kobo toolbox. It was then extracted and analyzed using SPSS version 26. Student's t-test was used to compare continuous variables, and the chi-squared test was used for categorical variables. Statistical significance was set at $P < 0.05$. Factors associated with COPD were determined by unadjusted logistic regression, and those with a P value <0.20 were considered for multivariable analysis.

3. Results

General characteristics of the study participants

During the study period, 232 PLWH were recruited. Ten participants were excluded from the study due to refusal to undergo spirometry. In contrast, nine were excluded due to their inability to follow directions and perform spirometry properly (n=4) or uninterpretable spirometry results (n=5). The remaining 213 participants were included, resulting in a response rate of 98.6%. Most of the study participants were 40-60, with a median age of 47 and a mean age of 45.5 years (SD±12.74). Most participants (69.5%) were female, and 44.1% were married. All but one participant was from an urban area. Fifty-six percent had normal BMIs. One-third had a primary education status, and 30% were government office employees.

Twenty-one (9.9%) participants were "ever" smokers, and 103 (48.4%) had a history of TB. Most PLWH (82.6%) had been living with HIV for > 10 years. All participants received a combination of ART, 164 (77%) of whom had received ART for > 10 years. Two hundred and six (96.7%) participants had a suppressed viral load, and 97.7% had a CD4 count ≥200 based on their most recent viral load result.

Table 1. The sociodemographic characteristics of the study participants who visited the ART Clinic of TASH from October 15-December 15, 2023

Demographic characteristics	Frequency	Percent (%)
Age of the study participants in years		
<40	60	28.2
40-60	130	61
>60	23	10.8
Sex of the study participants		
Male	65	30.5
Female	148	69.5
Marital status		
Single	82	38.5
Married	94	44.1
Widowed	37	17.4
BMI		
Underweight	22	10.3
Normal	120	56.3
Overweight	49	23
Obese	22	10.3
Education level		
No formal education	18	8.5
Primary	68	31.9
Secondary	62	29.1
Collage and above	65	30.5
Occupation		
Government employee	64	30
Housewife	64	30
Private employee	42	19.7
Merchant	17	8
Others	26	12.2
Residence		
Urban	212	99.5
Rural	1	0.5

Respiratory symptom-related characteristics of the participants

Of the study participants, 57 (26.8%) had a complaint of cough on most days, and among those who had a cough, 31.6% experienced it at night. Forty-eight (22.5%) patients had a chronic cough. Approximately 41% had complaints about shortness of breath, and 90.4% of them had shortness of breath, according to the modified Medical Research Council (mMRC) dyspnea scale score of two or more. Thirty (14.1%) participants had a history of chronic phlegm or mucus production, and nine (4.2%) had wheezing.

Behavioral characteristics of the participants

In this study, 21 (9.9%) participants were “ever” smokers and more than half (52.4%) had smoked cigarettes for ≥20 years, with a mean pack year of 16 years ±12 . There were no passive smokers identified. Thirty-one percent of the study participants had indoor biomass fuel exposure, while 66.6% had outdoor biomass fuel exposure. Nineteen percent of the study participants used kerosene for cooking, while 89.7% used electricity. Approximately 32% slept in the same room as the kitchen, while 38.5% had separate houses with a kitchen.

Table 2. Respiratory symptom-related characteristics of the study participants

Respiratory symptoms	Frequency	Percent
Have coughed several times on most of the day		
Ye	57	26.8
No	156	73.2
Timing of cough (n=57)		
Wakes up with a cough	4	7
In the morning	7	12.3
Throughout day and night	8	14.1
During the night	18	31.6
During the day	20	35.1
Chronic cough		
Yes	48	22.5
No	165	77.5
Cough with exertion		
Yes	23	10.9
No	190	89.2
Bring phlegm or mucus on most days.		
Yes	30	14.1
No	183	85.9
Timing of phlegm production (n=30)		
In the morning	27	90
Day time	3	10
Wheeze or have any whistling on the chest		
Yes	9	4.2
No	204	95.8
Get out of breath more easily than others your age		
Yes	88	41.3
No	125	58.7
The best description of the breathing situation (mMRC scale)		
Breathlessness only on strenuous exercise	8	3.8
Run out of breath when hurrying on the level or walking up a slight hill	62	29.1
Walk slower than most people on the level or stop after 15 minutes of walking	14	6.5
Stop for breath after walking approximately 100 meters	3	1.4
Too breathless to leave the house, or breathless when undressing	1	0.5
No shortness of breath	125	58.7
Have a period of increased shortness of breath with worsened cough with or without sputum during the last 12 months (exacerbations)		
Yes	15	7
No	198	93

Table 3. Behavioral characteristics of the study participants

Variable	Frequency	Percent
Smoking history (ever smokers)		
Yes	21	9.9
No	192	90.1
Duration of smoking in years (n=21)		
≤10	6	28.6
11-20	4	19
>20	11	52.4
Consume tobacco products other than cigarette		
Yes	2	0.9
No	211	99.1

Respiratory tract disease and comorbidity-related characteristics

In this study, 99 (46.5%) participants were treated for pulmonary TB in the past, and 1.9% received treatment for extrapulmonary TB at enrollment. Twelve (5.6%) patients had a history of COVID-19 infection. More than seven percent (7.5%) had a history of allergy; of those patients, 25% had allergic sinusitis. Fifty-two percent of participants reported a treatment history for chest infections, with 78.4% having two or more treatment histories. Approximately two percent (1.9%) of the participants had recurrent pulmonary problems during childhood. Forty-four (20.7%) patients had other comorbid illnesses, and among those patients, 49.7% had hypertension and were on treatment.

Table 4. Respiratory tract disease and comorbid illness characteristics

Parameters	Frequency	Percent
History of Tuberculosis		
I have active TB now (all extrapulmonary)	4	1.9
Could not Remember	10	4.7
Treated in the past	99	46.5
Never Treated	100	46.9
COVID 19 infection		
Yes	12	5.6
No	201	94.4
Allergy		
Yes	16	7.5
No	197	92.5
Types of allergies (n=16)		
Sinusitis	4	25
Eczema	4	25
Dermatitis	2	12.5
Rhinitis	2	12.5
Asthma	2	12.5
Medication allergy	2	12.5
History of chest infection and treatment		
Yes	111	52.1
No	102	47.9
Frequency of chest infection (n=111)		
One time	24	21.6
Two times	87	78.4
Pulmonary problems in childhood		
Yes	4	1.9
No	209	98.1
Comorbidities		
Yes	44	20.7
No	169	79.3

HIV/AIDS-related characteristics of the study participants

Of the study participants, 176 (82.6%) had been living with HIV for > 10 years. Of all participants who received combination ART, 164 (77%) had taken ART for > 10 years. Two hundred and six (96.7%) patients had a suppressed viral load, and 208 (97.7%) had a CD4 concentration ≥200 based on their most recent viral load. Six percent of the study participants were admitted to the hospital in the last two years.

Table 5. HIV/AIDS-related characteristics of the study participants

Variable	Frequency	Percent
Duration of HIV/AIDS in years		
<5	12	5.6
5-10	25	11.7
>10	176	82.6
CD4 count		
<200	5	2.3
>200	208	97.7
Viral load		
Suppressed	206	96.7
Not suppressed	7	3.3
Duration of ART in years		
<5	11	5.2
5-10	38	17.8
>10	164	77
Types of ART drugs used		
TDF+3TC+DTG[1]	177	83.1
AZT+ 3TC+ATV/RTV[2]	20	9.4
ABC+3TC+DTG[3]	8	3.8
TDF+3TC+EFV[4]	8	3.8

[1]TDF-Tenofovir, 3TC- Lamivudine, DTG- Dolutegravir
[2]AZT- Azidothymidine (Zidovudine), ATV- Atazanavir, RTV- Ritonavir
[3]ABC- Abacavir
[4]EFV- Efavirenz

Spirometry profiles, prevalence, and severity of COPD among PLWH

Among the study participants, 11 (5.1%) had an FEV1/FVC ratio <0.7. These individuals underwent post-BD spirometry, after which 10/213 (4.7%) met the ERS/ATS criteria for chronic obstructive lung disease [28]. Of these, seven out of ten were in GOLD Stage 2, two out of ten were in GOLD Stage 3, and one out of ten was in GOLD Stage 1. No study participant had ever had spirometry performed before.

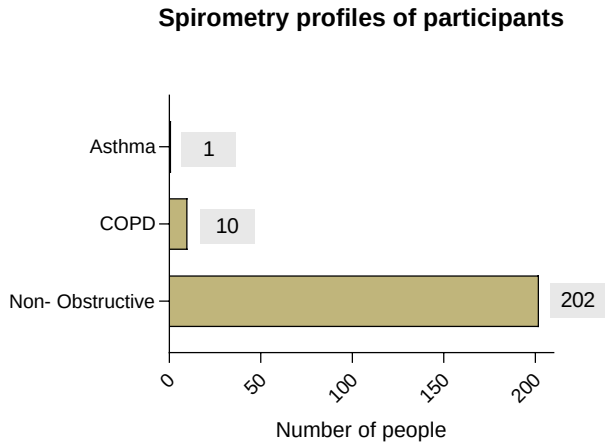

Figure 1. The spirometry profiles of participants

Factors associated with COPD in PLWH

This study measured associations using odds ratios and 95% confidence intervals. Accordingly, having a chronic cough, bringing up phlegm, having phlegm production without a cold, and smoking history were associated with COPD according to bivariate adjusted logistic regression. After conducting multivariable logistic regression, we

found that participants who had chronic cough were 4.4 times more likely to have COPD than those in the opposite compartment (AOR=4.4, [$CI_{95\%}$= 1.77, - 25.33]), and study participants who smoked cigarettes were 8.5 times more likely to have COPD than nonsmokers were (AOR=8.5, [$CI_{95\%}$ = 1.21- 60.13]).

Table 6. Unadjusted and adjusted logistic regression results for COPD and independent variables among PLWH

Variables	COPD		P value (bivariate)	COR ($CI_{95\%}$)	P value(multivariate)	AOR with 95%CI
	Yes	no				
Gender						
Male	6	59				
Female	4	144	0.051	0.27(0.07, 1.01)	0.843	1.2 (0.18, 8.26)
Cough several times on most days						
Yes	7	50	0.006	7.1(1.79, 28.66)	0.045*	4.4 (1.77, 25.33)
No	3	153				
Have phlegm or mucus on most days						
Yes	5	25	0.003	7.1(1.92, 26.35)	0.867	1.3(0.08, 19.16)
No	5	178				
Phlegm or mucus without cold						
No	6	186				
Yes	4	17	0.004	7.3(1.87, 28.39)	0.365	5.9 (0.13, 68.55
Wheeze or whistling in the chest						
No	9	195				
Yes	1	8	0.171	2.7(0.31, 24.05)	0.074	2.4 (0.12, 19.42)
Ever smoked						
Yes	5	16	0.000	11.7(3.06, 44.66)	0.031*	8.5 (1.21, 60.13)
No	5	187				
CD4 count						
<200	1	4	0.144	5.5(0.56, 54.63)	0.241	2.8 (0.45, 32.14)
>200	9	199				
Viral load suppression						
Yes	9	197				
No	1	6	0.253	3.6(0.39, 33.59)	0.249	4.1 (0.49, 45.34)

*Statistically significant association

4. Discussion

Ethiopia, a sub-Saharan country, has one of the highest prevalences of HIV. However, there is currently no data on this population's prevalence and factors associated with COPD. Our study aimed to bridge this gap and determine COPD's prevalence and related factors. In this study, we observed a prevalence of COPD of 4.7% [CI95% = 2.0, - 8.0]. Furthermore, we identified that self-reported chronic cough and smoking were independently associated with COPD. We did not find any associations between COPD and TB treatment, biomass fuel use, time since HIV diagnosis, COVID-19 infection, treatment, recurrent chest infection, or other respiratory symptoms.

The median age of our study participants was 47 years, which is consistent with the results of a systematic review of 30 studies globally reporting a median age of 33-57 years [15]. The median age of participants from various African studies is also comparable to that of our study participants, ranging from 45 to 47 years [1,16,17].

In this study, we found that most of our PLWH had been followed up for more than ten years (82.6%) at our clinic, among whom 96.7% had a suppressed viral load and 97.7% had a CD4 count > 200. However, more than half of the participants reported one or more chronic respiratory symptoms (dyspnea, 39.9%; chronic cough, 22.5%; chronic phlegm production, 14.1%; and wheezing, 4.2%). We observed that participants with chronic cough were more likely to have COPD than those without chronic cough (AOR=4.4, [95% CI=1.77, - 25.33]). In their systematic review of 24 studies spanning from 1946 to 2015, James Brown et al. reported a high prevalence of respiratory symptoms despite patients receiving effective ART [18]. A similar study performed in Cameroon by Pefura Yone and colleagues estimated the prevalence of respiratory symptoms to be 47.5% among PLWH in urban Cameroon [17]. Akanbi and his colleagues, in their cross-sectional study in an urban Nigerian tertiary center, found the prevalence of respiratory symptoms in their cohort was 17.6% (dyspnea 11.1%, cough 7%, phlegm production 5.1% and wheezing 4.5%), with the current HIV status of the participants mirroring our findings, with close to 98% taking ART, with ≥ 90% of the participants having a CD4 count > 200(1). In a similar study in Uganda, investigators found that 45% of the participants had at least one chronic respiratory symptom (cough 30%, shortness of breath 26%, wheezing 21%, and phlegm production 21%) [16]. A high burden of respiratory symptoms is associated with reduced health-related quality of life even without a confirmed COPD diagnosis [19]. A European Community Respiratory Health Survey demonstrated that respiratory symptoms were common and associated with reduced quality of life, increased risk of developing future disease, a rapid decline in lung function, and increased mortality [20,21,22]. These findings highlight our findings of a high burden of respiratory symptoms and suggest an emphasis on screening and close follow-up of this specific group of patients.

Smoking is an important contributing factor to the

major burden of COPD worldwide. In our study, 9.9% of participants were ever smokers, with more than half having smoked for > 20 years. This finding is in line with those from other studies that reported smoking as an associated factor with COPD in PLWH. Notably, the smoking prevalence in these cohorts ranged from 50-60% [23,24]. Our results contrast with reports from other African countries. For instance, a study in Cameroon showed that even though 12% of participants were smokers, smoking was not associated with developing COPD [17]. Similarly, Akamai et al. reported that the prevalence of smoking was 17.1%, and smoking was not associated with an increased risk of COPD [1]. Similarly, in a cross-sectional study from Uganda, the prevalence of smoking was 24%, and smoking was not associated with COPD [16]. This difference from our study may be related to the relatively lower number of packs smoked and the shorter duration of smoking in those studies [1,16,17].

PLWH frequently suffers from TB, often from recurrent episodes. Multiple studies have shown that a history of TB is associated with COPD [25]. In our cohort, 48.3% had a history of TB, which is comparable to other studies, such as one in Cameroon that reported 42.1% of their cohorts previously having TB. Our findings are much greater than those reported in Nigeria and Uganda, with 23% and 25% of TB, respectively [1,16]. In our study, a history of TB was not associated with developing COPD, similar to the findings of a study performed in Nigeria [1]. In studies reported from Uganda and Cameroon, TB history was one of the factors associated with COPD, which differs from our results [1,17].

Several studies have reported that a low BMI is associated with developing COPD [16,17,25]. In our study, 10.3% of the participants had a low BMI, and 33.3% of the participants had a BMI ≥25; however, BMI of any degree was not correlated with COPD.

The prevalence of COPD in our study was 4.7%, which is lower than that in reports from American and European cohorts, in which the prevalence ranged from 9 to 17.2% [23,26,27]. This difference in prevalence across cohorts may be explained by a disproportionately high percentage of smoking, as high as 60%, compared to 9.9% in our study. Although our patients were exposed to biomass fuel, almost all were urban dwellers, with significantly less contact and exposure to biomass fuel than people living in rural areas, which did not alter the risk of the cohorts to COPD. The 4.7% prevalence of COPD in our cohort is greater than that reported in Uganda (3.1%), a setting quite similar to Ethiopia [16]. A previous history of TB, self-reported history of shortness of breath, and BMI ≤ 21 were associated with COPD in the Ugandan Cohort, while only smoking history and self-reported chronic cough were associated factors identified in our study [16]. Reports from Western Africa have shown a COPD prevalence ranging from 2.2% in Cameroon to 15.4% in Nigeria [1,17]. Factors such as previous history of TB, low BMI, and chronic respiratory symptoms were associated with COPD in a study from Cameroon [17], whereas only age > 50 years was independently associated with COPD in the Nigerian cohort [1]. Although the study setting for the Nigerian cohort resembles ours, only 64.5% of their participants had a suppressed viral load [1] compared to 96.7% of our participants, which may explain differences in COPD prevalence. This could also generate further evidence that achieving a suppressed viral load with an appropriate ART regimen could help prevent COPD by decreasing airway inflammation.

To our knowledge, this is the first study in Ethiopia that aimed to assess the prevalence and associated factors of COPD. Despite the low prevalence of smoking in our country, PLWH who smoke were more likely to develop COPD, and more than half of the participants had ≥ 1 chronic respiratory symptom. Participants diagnosed with COPD had never undergone a spirometry assessment before enrollment and were unaware of their condition at the time of the study. Performing spirometry for all the study participants and using a post-BD FEV1 result to define COPD was one of the study's strengths.

Limitations of the study

The study was conducted in a single tertiary center, making generalizing our results to larger and broader populations outside of Addis Ababa challenging. Due to the study's cross-sectional nature, we could not assess the impact of ART on the timing and prevalence of COPD diagnosis. Our study's lack of chest imaging (X-rays or computed tomography scans) limited our ability to exclude potential differentials for obstructive physiology and further describe radiologic variants.)

Conclusion

In this study, the prevalence of COPD was 4.7%, and the odds of COPD were associated with a history of smoking and a self-reported history of chronic cough in multivariable models. This study also emphasizes the importance of early screening of symptomatic patients and performing spirometry to establish a diagnosis of COPD.

Abbreviations

AOR-Adjusted odds ratio

ART-Antiretroviral therapy

ATS-American thoracic society

BD- bronchodilator

BMIs- Body Mass Indexes

CI-Confidence Interval

COPD- chronic obstructive lung disease

COR- Crude odds ratio

COVID19-Coronavirus disease 2019

ERS-European respiratory society

FEV1-Forced expiratory volume at the first second

FVC-Forced vital capacity

GOLD- Global initiative for chronic obstructive lung disease

NCD- noncommunicable disease

PLWH- People living with HIV

SD- Standard deviation

TB-Tuberculosis

WHO-World health organization

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