IJPSR (2022), Volume 13, Issue 4 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 26 June 2021; received in revised form, 06 August 2021; accepted, 14 August 2021; published 01 April 2022

DRUG UTILISATION PATTERNS, PREVALENCE OF RISK FACTORS, OPPORTUNISTIC INFECTIONS AND QUALITY OF LIFE AMONG HIV PATIENTS IN A GOVERNMENT HOSPITAL IN BHIMAVARAM

Roopa Pravallika Koduri, Akhila Kombathula, Kumar VS Nemmani, Jakka Venkata Srinivas and Anil Kumar Sagi *

Department of Pharmacy Practice, Shri Vishnu College of Pharmacy, Bhimavaram - 534202, Andhra Pradesh, India.

Keywords:

HIV, Anti-retroviral therapy, quality of life, Tuberculosis, Opportunistic infections.

Correspondence to Author:
Mr. Anil Kumar Sagi

Assistant Professor,
Department of Pharmacy Practice,
Shri Vishnu College of Pharmacy,
Bhimavaram - 534202, Andhra Pradesh, India.

E-mail: anilkumar@svcp.edu.in

ABSTRACT: Objectives: To assess the risk factors, opportunistic infections (OI's), prescribing patterns along with ADRs, medication adherence, and quality of life (QoL) among HIV patients. **Methods:** This is an Ambi-directional cohort study conducted at the Government hospital, Bhimavaram, for 6 months from July 2019 to December 2019, including 201 HIV patients' data. The data were analyzed using GraphPad Prism 8.3.0. Descriptive statistics & paired t-test were employed to assess risk factors, OIs, prescribing patterns, and QoL, respectively. **Results:** Out of 201 patients. Heterosexuality (96%) was found to be a predominant risk factor in this study. Between type-1 and type 2 HIV patients, Tenofovir Disoproxil Fumarate/ Lamivudine & Efavirenz (TLE) and Tenofovir Disoproxil Fumarate/ Lamivudine/ Lopinavir/ Ritonavir (TL/ATV/r) were the first-line and second-line therapies respectively in type-1 patients; however, TL/LPV/r was reserved for type 2 individuals. Among 201 patients, 55 patients were reported with 60 ADR's and the predominant ADR was found to be rashes (36%). Approximately 76% were reported with a history of OI's, the most prevalent being TB (39%). Almost 94% of individuals were highly adherent to ART with the improvement in QoL after treatment. **Conclusion:** This study concluded that heterosexuality is the major risk factor and is effectively managed by TLE-based ART. It also reported rashes as the most common ADR and TB as the most prevalent OI. QoL in all domains has been improved after ART with greater adherence.

INTRODUCTION: The global incidence-prevalence ratio of the human immunodeficiency virus (HIV) has declined from 11.2% in 2000 to 6.6% in 2010 to 4.6% in 2018, AS per United Nations Programme On HIV/AIDS (UNAIDS). According to WHO, globally 37.9 million people are living with HIV [1]. The adult prevalence of HIV was estimated to be 2.1 million as per the National AIDS control program (NACO) in India [2].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.13(4).1632-39

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.13(4).1632-39

AIDS is caused by an RNA retrovirus called the human immunodeficiency virus (HIV). Two forms of HIV have been described; they are HIV type 1 and HIV type [2]. Clinical presentations in these

patients often have an illness with fever, pharyngitis and adenopathy, which may last for 2 weeks. Both HIV1 and HIV2 are zoonotic infections, and their origin can be traced to a species of chimpanzees [3]. Infection with HIV occurs through three primary modes: sexual, parenteral and perinatal. Currently, HIV treatment is recommended for all persons living with HIV (PLWH) [4].

There are multiple first-line antiretroviral therapy (ART) regimens recommended for treatment-naïve PLWH [5]. At present, the HAART should contain one Non-NRTI (either Nevirapine (NVP) or Efavirenz (EFV)) plus two NRTIs (lamivudine or Emtricitabine or Zidovudine (AZT) or Tenofovir Disproxil Fumarate (TDF)) [9]. This is applicable for those who have CD4 count ≤ 350 cells / mm^3 and clinical staging in adult stages 1 and 2 as per WHO recommendations [6]. Adverse reactions and medication non-adherence are seen in patients who are under ART drugs; these are found to be the reasons for switching or discontinuing the regimen. Stevens-Johnson Syndrome (SJS), rashes, and hepatotoxicity are mostly seen in adverse drug reactions (ADRs) with the use of nevirapine6. Identifying risk factors for ADRs is of crucial importance to optimize the initial choice of ARVs regimen before initiating therapy [7, 8]. Though HIV is the initial causative agent, most morbidity and mortality rates result from opportunistic infections (OIs) [9].

The most common OIs are Tuberculosis (TB), oropharyngeal candidiasis, CNS diseases, sepsis, bacterial pneumonia, Kaposi's sarcoma, and lymphoma. The in-time intervention of OIs, helps individuals to live longer [10]. The current study sets out to use the WHOQOLHIV BREF questionnaire, a newly-developed, multi-dimensional instrument comprising 26 items that will facilitate effective comparison within the QOL domains. In considering the initial identification of AIDS in the United States in 1981, formidable advancements have taken place in the insight of this fearful disease. But attempts at finding its treatment and a vaccine have not yet succeeded. Hence the global attention is presently focussed on preventive measures. As AIDS is a more prevalent disease. This study aims to focus on evaluating current ART prescribing patterns, their ADRs, and keeping keen observation on medication adherence, and assessing their QOL.

MATERIALS AND METHODS:

Study Site and Population: The study was an Ambi-directional cohort study carried out over six months from July 2019 to December 2019. This study was conducted in the ART Centre, Government hospitals, Gandhi Nagar, Bhimavaram, West Godavari district, Andhra Pradesh-534202, India. This hospital provides primary and specialized health care facilities to people in and around Bhimavaram. Patients who are willing to participate in the study with age > 18 years of either gender were included. This study excluded patients who are not willing to participate in the study.

Data Collection: Patients who were coming to the hospital regarding the disease in the outpatient department were screened based on the inclusion and exclusion criteria. Subjects who met the inclusion criteria were enrolled for the study. Informed consent was obtained from the patients. Details regarding the past medical history, medications, current therapy, their quality of life by using questionnaires were obtained by patient interview and by observing case notes. Symptoms, risk factors, and prescribing patterns of the patients were obtained by using a data collection form, and it was documented. The drug charts provided information on the type of the ART regimen, percentage of medication adherence, and the CD4 cell count, ADR's or History of opportunistic infections if any were reported.

Ethical Considerations: The study was started after obtaining clearance from the institutional ethical committee. All the information collected from the participants was strictly used only for research purposes, and confidentiality was maintained.

Assessment of Health-Related Quality of Life: According to the study design, a patient's health-related quality of life was measured by using the scale WHOQOL-BREF for HIV. The collection of patient health-related issues according to their quality of life was done using appropriate questionnaires and assessed using scores according to scale. There are a total of 26 items under four

domains. Domain I consists of 7 questions, Domain II with 6 questions, Domain III with 3 and Domain IV with 8 questions with a score range from 1 (poor performance) and 5 (excellent performance).

Statistical Analysis and Interpretation: All statistical analysis were performed using Graph Pad Prism 8.3.0 (San Diego, California, USA). Data were entered into Excel (version 2010). Descriptive statistics of socio-demographics and clinical variables included percentages, mean and standard deviation. The prescribing patterns of antiretroviral treatment were evaluated. Mean scores before and after treatment and mean changes were calculated for the domains of the WHOQOL-BREF questionnaire. A paired t-test was used to determine if the change detected from pre and post-treatment was significant. The probability value of ≤ 0.05 was set AS significant and ≤ 0.001 as highly significant.

TABLE 1: DEMOGRAPHICS

Parameter	No. Of Individuals (N=201)	Percentage of Individuals (%)
Age group (in yrs)		
Less than 20	6	3
21-30	47	23
31-40	75	37
41-50	49	25
51-60	22	11
More than 60	2	1
Gender		
Female	104	52
Male	97	48
Education		
Illiterate's	105	52
Primary	42	21
Secondary	39	19
College	15	8
Marital status		
Married	164	82
Widowed	29	14
Single	8	4
Type of HIV		
HIV-1	197	98
HIV-2	4	2
Risk Factors		
Heterosexual	192	96
Mother to child	5	2
Blood Transfusion	3	1.49
MSM	1	0.49

RESULTS & DISCUSSION:

Sociodemographic Data and Risk Factors: A total of 201 HIV-positive individuals were enrolled in this study. Around 37% of the patients were in the age group of 31-40 years. Most of them were female (52%), and more than 50% were illiterates. Almost three-fourths of HIV-positive individuals were HIV type 1, and 82% of them were married. Heterosexuality (96%) is found to be the predominant risk factor/route of transmission followed by others, and the least is found to be Men having sex with Men 0.49% **Table 1.** The studies conducted by Paranjape and Challacombe (2016), have shown heterosexuality to be the predominant one [10]. However, it is followed by injecting drug users, commercial sex workers, and men having sex with men. The risk factor pattern identified in this study is not similar to other studies, where injecting drug users, homosexuality, and commercial sex workers are at lower rates in this locality.

In Type-1 patients, TLE (83%) is most commonly used as first-line therapy followed by ZLE (14%) whereas TL/ATV/r is a second-line therapy **Fig. 1a.** and in type 2 individuals, TL/LPV/r is the only most commonly prescribed combination in our respective government hospitals **Fig. 1b.** Among 197 type-1 patients, ZLN use is comparable to TLE in 2016 whereas in the later years ZLN use is decreased with a steep rise in TLE usage in 2019 from **Fig. 2.** However, among 28 individuals of ZLN use, the shift from ZLN to TLE is predominant (39%) when compared to others **Fig. 3.** This is in correlation with the study conducted by Parmar because they found that HIV infected patients taking Efavirenz based HAART (TLE) had better clinical outcomes, higher survival rate, and increase in CD4 cell count after the HAART ($p=0.001$) compared to those taking Nevirapine based HAART (ZLN) [11]. In addition to efficacy, ADR's were found to be predominant with NVP based therapy [12]. However, a study conducted by Bhuvana and Hema shows that ZLN is the most commonly prescribed regimen which is not by this study[13].

Prevalence of Adverse Drug Reactions: Among 201 patients, 55 individuals reported 60 ADRs in which most predominant is found to be rashes (36%) which is attributed to NVP based therapy

(ZLN) assessed using casualty assessment scale (Naranjos Assessment Scale) where we can optimize the initial ART regimen based on the ADR's reported followed by dizziness (20%), Nausea & Vomiting (17%) and least is Insomnia (8%). Miscellaneous is about 18% which includes orthostatic hypertension, anorexia, profuse sweating, vertigo, *etc.* **Fig. 4.** Unlikely the studies conducted by Sarraf & KB have shown that along with skin rash, other ARDs like anemia, nausea, and vomiting were also reported as the most common ADRs. These ADRs were observed with TLE, whereas in this study, the reported ADRs were associated with ZLN14, [15]. However, another study reports that anemia is the most commonly reported ADR due to the use of Zidovudine, which is not similar to this study because initially, they screen for hemoglobin count to start ZLN to ensure further complications based on the range they prioritize the ARV regimen [16].

Prescribing Patterns in HIV Type 1 and Type 2:

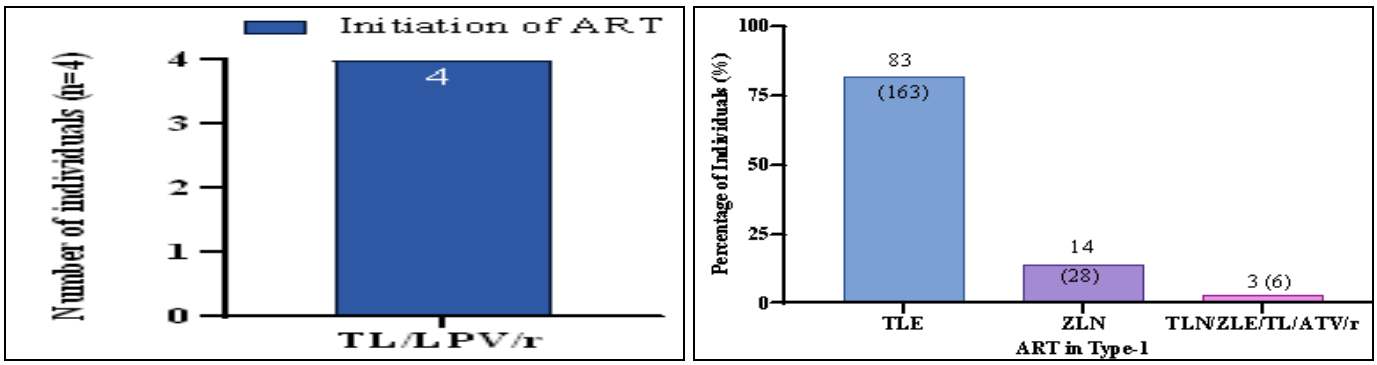

FIG. 1A & 1B: COMBINATIONAL ANTI-RETROVIRAL THERAPY IN HIV TYPE 1 & TYPE 2 PATIENTS. TLE- Tenofovir Disoproxil Fumarate/ Lamivudine & Efavirenz, **ZLN-** Zidovudine /Lamivudine & Nevirapine, TLN: Tenofovir Disoproxil Fumarate/ Lamivudine & Nevirapine, **ZLE-** Zidovudine /Lamivudine &Efavirenz, TL/ATV/r- Tenofovir Disoproxil Fumarate/Lamivudine/Atazanavir /Ritonavir, TL/LPV/r- Tenofovir Disoproxil Fumarate/Lamivudine/Lopinavir/Ritonavir. (Values within the bar indicates number and values outside the bar indicate percentage).

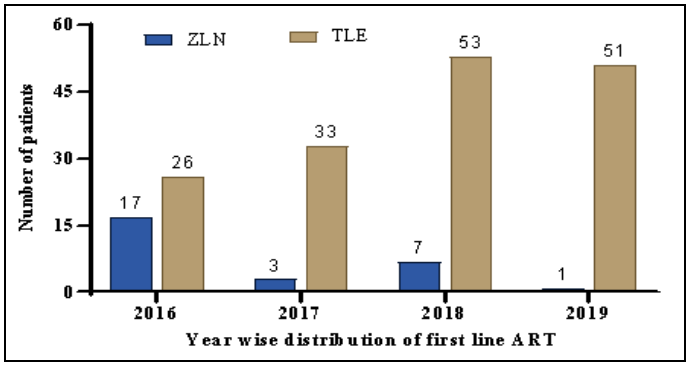

FIG. 2: YEAR-WISE PRESCRIPTION OF TLE & ZLN IN TYPE 1 PATIENT. Values within the bar indicates number, and values outside the bar indicate percentage).

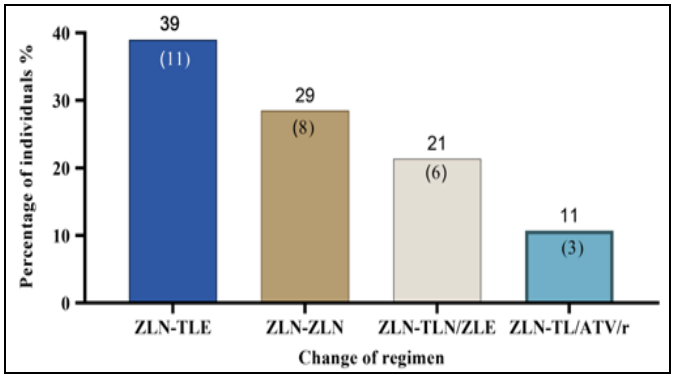

FIG. 3: SHIFT OF REGIMEN WITH THE USE OF ZLN. Values within the bar indicates number and values outside the bar indicate percentage).

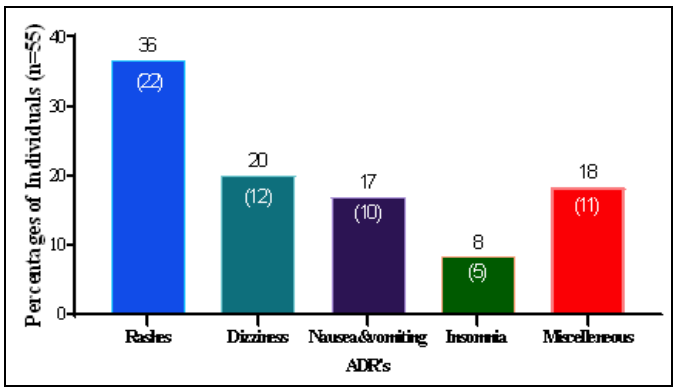

FIG. 4: PREVALENCE OF ADVERSE DRUG REACTIONS. Miscellaneous: orthostatic hypertension, anorexia, profuse sweating, vertigo (Values within the bar indicates number and values outside the bar indicate percentage).

Prevalence of Opportunistic Infections (Oi's): In this study 24% didn't have any history of OI's whereas in about 76% the most prevalent OI is found to be TB (39%) followed by Diarrhea (10%), whereas Herpes Zoster and Upper Respiratory Tract, Skin Infections were equally comparable, However, the least is found to be Urinary Tract Infections (3%) & candidiasis (2%) **Fig. 5.** Whereas the studies conducted by Melkamu, Rajput, and Solomon reported TB (29.8%) was the most common OI, which is similar to the study conducted by [9, 17, 18].

The main factors associated with it are CD4 count less than 200 cells/mm3 and sometimes CD4 count more than 500 cells/mm3 and HIV patients on WHO stage II-IV & poor ART adherence. From **Fig. 6a**, 94% are with high medication adherence.

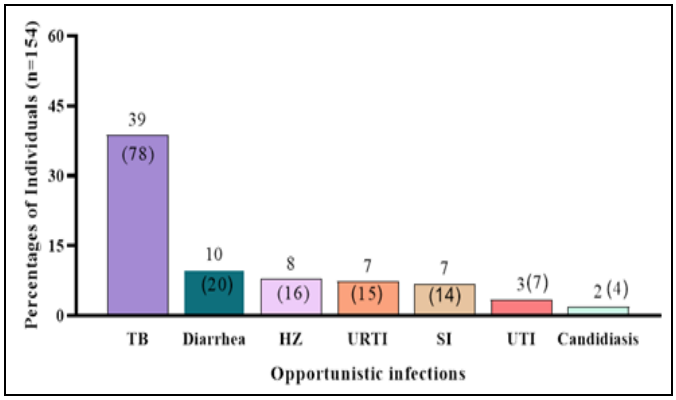

FIG. 5: PREVALENCE OF OI'S. TB- Tuberculosis, **HZ**- Herpes Zoster, **URTI**- Upper Respiratory Tract Infections, SI- Skin Infections, UTI- Urinary Tract Infections (Values within the bar indicates number, and values outside the bar indicate percentage).

Medication Adherence:

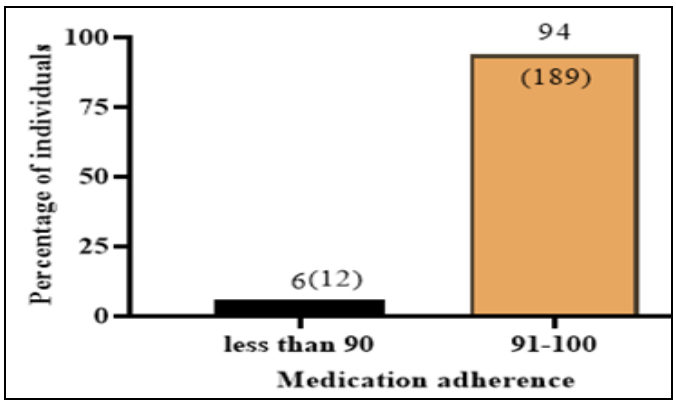

FIG. 6A: MEDICATION ADHERENCE IN HIV PATIENTS. Values within the bar indicate number, and values outside the bar indicate the percentage.

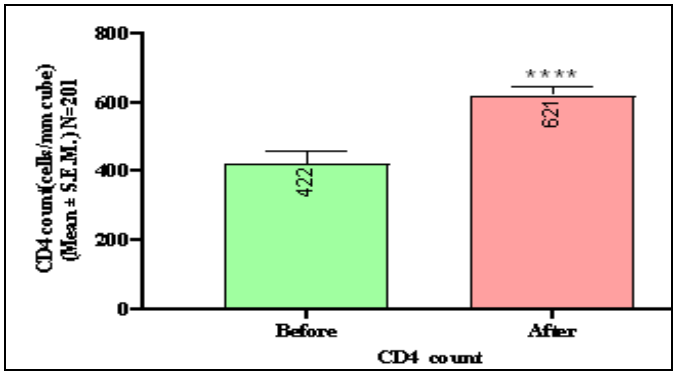

FIG. 6B: CD4 CELL COUNT BASED ON PRE AND POST ART THERAPY

Quality of Life: Different domains of life have been assessed and compared using their mean values, in which the mean value of physical health before treatment is 19.24 and after treatment is 25.07. The difference in means is highly (statistically) significant ($p < 0.001$). The mean psychological score pre-treatment is 15.59, and post-treatment is 20.55. The difference in means is highly (statistically) significant ($p < 0.001$). However, the mean social relationship between pre-treatment and post-treatment was found to be non-significant. The mean environment score pre-treatment is 26.55 and post-treatment is 30.60. The difference in means is highly statistically significant (P=0.001) **Table 2.** This shows that there is an improvement in the quality of life post-treatment. The response score of all scales increased significantly, which indicates the improvement in the quality of life after treatment. **Fig. 7** suggest that overall QoL has been improved greatly in physical health (19.24 ± 0.31, 25.07 ± 0.20), psychological (15.59 ± 0.30, 20.55 ± 0.18) and environmental domains (26.55 ± 0.21, 30.60 ± 0.21) with the use of ART, because more than 50% of individuals were illiterate's contributing to one of the reasons. This correlates to the studies conducted by Desta & Ahmed, which shows that among the assessed domains, the largest proportions of participants scored high QoL in Spiritual, religious, personal beliefs followed by a psychological domain. On the contrary, many of the participants scored least in the social relationship domain, which was according to the study discussed above [22, 23]. This reveals the importance of assessing the HRQOL among HIV patients to ART monitoring.

TABLE 2: DOMAIN WISE QOL IN HIV PATIENTS BASED ON WHOQOLBREF QUESTIONNAIRE

DOMAIN	Mean ± SEM		NUMBER OF QUESTIONS	SIGNIFICANCE
Physical health (3, 4, 10, 15, 16, 17, 18)	Before	19.24 ± 0.31	7	p < 0.001****
	After	25.07 ± 0.20		
Psychological (5, 6, 7, 11, 19, 26)	Before	15.59 ± 0.30	6	p < 0.001****
	After	20.55 ± 0.18		
Social relationship (20, 21, 22)	Before	10.21 ± 0.15	3	p < 0.05*
	After	10.51 ± 0.15		
Environment (8, 9, 12, 13, 14, 23, 24, 25)	Before	26.55 ± 0.21	8	p < 0.001****
	After	30.60 ± 0.21		

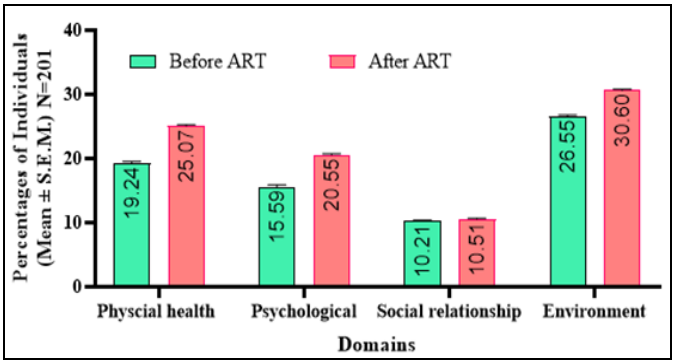

FIG. 7: OVERALL QOL IN HIV PATIENTS BASED ON WHOBREF QUESTIONNAIRE

CONCLUSION: In this study age group of 31-40 years are more affected, mostly by heterosexuals (96%), and females are greater in number than males. It concludes that EFV-based HAART has better clinical outcome than NVP, in which the most prevalent OI is found to be TB, and 48% HAART-related ADRs were recorded among which skin rashes is predominant. High adherence is predominant in most of the HIV-infected individuals which are found to be significant ($p < 0.001$) and also QoL is improved in all domains

which show greater therapeutic efficacy to the ART regimen. A major limitation of this study is the absence of a randomly selected group, which could have led to selection bias towards those who are more likely to have a positive test result and to certain types of combinational drugs, where the banned drugs like SLN/SLE are omitted from data recruitment. However, case profiles registered after the year 2014 have been collected.

ACKNOWLEDGEMENT: We thank the management, doctors, and staff of government hospitals for providing all facilities required to undertake the study. We also thank Dr. Kumar. V. S Nemmani, Director & Dr. K. Prasad, Principal, Shri Vishnu College of Pharmacy, Bhimavaram, for their cordial support. We also express our deep gratitude & regards to Mr. Venkata Srinivas Jakka, Assistant Professor, Department of Pharmacy Practice, Shri Vishnu College of Pharmacy, Bhimavaram.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CONFLICTS OF INTEREST: No competing interest declared.

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How to cite this article:
Koduria RP, Kombathulaa A, Kumar VSN, Sagia AK and Srinivasa JV: Drug utilisation patterns, prevalence of risk factors, oppurtunistic infections and quality of life among hiv patients in a government hospital in bhimavaram. Int J Pharm Sci & Res 2022; 13(4): 1632-39. doi: 10.13040/IJPSR.0975-8232.13(4).1632-39.