Original Research Article

FREQUENCY OF AIDS DEFINING OPPORTUNISTIC INFECTIONS IN HOSPITALIZED HIV INFECTED PATIENTS

BACKGROUND: Human Immunodeficiency virus patients with AIDS defined opportunistic infections with Pneumocystis jiroveci, cryptoccocal, disseminated TB, cytomegalovirus, and cytomegalovirus associated retinitis, and cryptospordiasis.
OBJECTIVE: To determine the frequency of AIDS defining opportunistic infections in hospitalized HIV infected patients.
METHODOLOGY: This cross sectional study was conducted from 21st October 2018 to 20th April 2019 at Department of Medicine, Civil Hospital, Karachi. Total 154 diagnosed patients of HIV were included. For diagnosis of various AIDS defining illness, clinical, radiological and bacteriological evidence of disseminated tuberculosis chronic cough, and weight loss diagnosed by AFB smear/ gene experts. Pneumocystis jiroveci was diagnosed by bronchoalveolar lavage and CD4 counts. Cryptosporidiosis with watery diarrhea and stool sample microscopy, cerebral toxoplasmosis with headache, hemiparesis, vomiting, diagnosed by serology and cytomegalovirus retinitis with blurred vision diplopia, vision impairment and Cryptococcal meningitis with fever >98.6oF. Headache, stiff neck, photophobia diagnosed by microscopy, culture, or antigen was done. Descriptive statistics were calculated and stratification was done. Post stratification chi square test was applied. P value ≤ 0.05 was taken as significant.
RESULTS: There were 71.4% male and 28.6% female patient. The mean HIV duration was 15.25±5.09 months. The overall mean CD4 count was 174.17±12.85/cumm. 18.8% patient were found with disseminated tuberculosis, 31.2% with pneumocystis pneumonia, 12.3% with cerebral toxoplasmosis, 18.2% with cryptococcal meningitis, 3.9% with cryptospordiasis and 14.9% with cytomegalovirus retinitis.
CONCLUSION: Pneumocystis pneumonia was the most prevalent infection followed by disseminated tuberculosis, cryptococcal meningitis, cytomegalovirus retinitis, cerebral toxoplasmosis, and cryptospordiasis.
KEYWORDS: Frequency, AIDS, Opportunistic Infections, Hospitalized HIV Patients

INTRODUCTION: In the summer of 1981, the Centers for Disease Control and Prevention reported unexplained cases of Pneumocystis jiroveci pneumonia and/or Kaposi's sarcoma in healthy gay males in New York and Los Angeles. Months, the disease was found in IDUs, transfusion recipients, and haemophiliacs. The epidemic's epidemiologic pattern revealed an infectious agent spread by sexual (gay and heterosexual) contact and blood or blood products as the most probable etiologic cause. In 1983, HIV was identified from a patient with lymphadenopathy, and in 1984, it was proven to be the etiology of AIDS.[(1)]

Cases of HIV/AIDS have been reported in nearly every nation. According to the joint UN HIV/AIDS programme, 33.2 million of people with HIV at the end of 2007. (UNAIDS). [(1)] More than 95 percent of HIV/AIDS patients live in low- and middle-income countries, and 2.5 million are children as young of 15.[(2)] In 1986, commercial sex workers (CSWs) in Tamil Nadu were first diagnosed with The disease. In 2006, the national adult HIV prevalence in India was estimated at 0.36 percent, or 2 to 3.1 million people, about half the previous estimate. Generally, female adult prevalence is 0.29 percent, while male prevalence is 0.43 percent. AIDS still threatens the cream of society, those in the prime of their working lives, with 88.7% of all infections occurring in those aged 15-49. Adult HIV prevalence is 0.36 percent in the general population, but higher in high-risk categories. It is 8.71 percent among IDUs, 5.69 percent among MSMs, and 5.38 percent among FSWs.[(3)]

The first HIV-positive Pakistani was found in 1987.[(4)] NIH, Islamabad, recognized 3325 patients through March 2010.[(5)] Viral replication is controlled by HIV-1 specific CD8+ T-cells (T-cells). Early in HIV-1 infection, the cytotoxic T-lymphocyte (CTL) response appears together with a fast decline in plasma viremia.[(6)]

Female sex workers (FSWs) were the biggest category of HIV high risk persons in Pakistan, estimated at 79127 with five sub-types. The next biggest category was injection drug users, followed by commercial sex workers and hijra sex workers (31555, 19320, and 14702).[(7)] According to the study's logic, cytotoxic T-lymphocytes' capacity to reduce viral load and affect illness prognosis differs across individuals infected with HIV-1. Opportunistic infections (OIs) were a major source of morbidity and death in HIV patients prior to antiretroviral medication. In the mid-1990s, the upscaling of ART resulted in a considerable decrease in OIs and hence an improvement in the HIV prognosis.[(8),(9)] The discovery and worldwide spread of HIV/AIDS is the greatest health threat of our time. In 2010, the WHO and UNAIDS estimated that 34 million individuals had HIV. In the same year, 2.7 million individuals got HIV and 1.8 million died of AIDS. [(10)]

Opportunistic infections (OIs) are infections that take advantage of a compromised immune system. Some OIs are used to designate HIV/AIDS phases.[(11)] Prior to the widespread use of strong combination antiretroviral treatment (ART), OIs were the leading cause of HIV morbidity and death. In one research, patients with a history of avoidable OIs died at a rate of 66.7 per 100 compared to 2.3 per 100 for those without.[(12)]

Despite this, fatality rates from OIs remain high, with one-third of patients presenting late (with a weakened immune system), not receiving HIV medication or healthcare, and not attaining optimal viral load suppression or immunological reconstitution despite appropriate ART.[(9), (13)] Some OIs may induce HIV progression, increasing susceptibility to infection and rates of HIV transmission.[(14), (15)]

OIs have indirect effects as well: certain OIs may accelerate HIV development, increasing vulnerability to new infections and HIV transmission rates.

PATIENT AND METHODS: The study was performed at the Department of Medicine, Dow University, Civil Hospital Karachi from six months from 21st October 2018 to 20th April 2019. Total 154 patients were included as calculated by taking previous reported prevalence of cryptosporidiosis HIV hospitalized patient as 3%,[121] confidence level 95% and margin of error of 2.7% as calculated by formula $n = [P(1-P)Z \times /2]/e^2$ (n = 154 patients) while the non-probability consecutive sampling technique was used to recruit the population. The inclusion criteria were age over 18- 60 years; both gender and all diagnosed hospitalized cases as per operational definition of HIV while the exclusion criteria patients with other concurrent infection prior to diagnosis of HIV, all outpatient HIV positive patients and those who were not give written consent for inclusion in the study.

HIV Definition: Patients found HIV serology positive and CD4 lymphocyte count <200 cells/mcl or < 14% were labeled as having AIDS.

AIDS Defining Opportunistic Infection: AIDS defining illness included following mentioned below, diagnosed clinically, radiologically and bacteriological evidence.

Pneumocystis Jiroveci: Cough, shortness of breath with respiratory rate >30/min, diagnosed by broncho alveolar lavage sent for histopathologic examination.

Cryptococcal Meningitis: Fever >98.6 oF, headache, stiff neck, photophobia diagnosed by microscopy, culture, or antigen.

Cytomegalovirus Retinitis: Blurred vision, diplopia, vision loss diagnosed by ophthalmoscopy or if required tissue biopsy.

Disseminated Tuberculosis: Defined by having chronic cough >2weeks and weight loss of >5-10kg in 1 month diagnosed by 3 consecutive specimens or gene experts identifying organism.

Cerebral toxoplasmosis: CNS symptoms confirmed by serological evidence of Toxoplasma on PCR.

Cryptosporidiosis: Watery diarrhea, weight loss, dehydration diagnosed by microscopy of stool sample.

Patients were selected on the basis of selection criteria, the risks and benefits of the study were explained to them and after their informed consent, a detailed per approved. Study was conducted after approval from ethical review committee from CPSP. Performa was filled as follows by the candidate only: Patient name, age, gender, admission number and history and physical examination were done and recorded. Patients with HIV diagnostic criteria were enrolled and for diagnosis of various AIDS defining illness clinical, radiological and bacteriological evidence of disseminated tuberculosis chronic cough & weight loss diagnosed by AFB smear/ gene experts, pneumocystis jiroveci with symptoms of cough, shortness of breath, diagnosed by bronchoalveolar lavage and CD4 counts, cryptosporidiosis with watery diarrhea and stool sample microscopy, cerebral toxoplasmosis with headache, hemiparesis, vomiting, diagnosed by serology and cytomegalovirus retinitis with blurred vision diplopia, vision impairment and Cryptococcal meningitis with fever >98.6 F, headache, stiff neck, photophobia diagnosed by microscopy, culture, or antigen were done by experienced doctor with working year of experience at least 4 years.

Data analysis was performed through SPSS Version-20. Descriptive statistics were calculated for quantitative variable like age, BMI, duration of HIV, CD4 count were presented as mean and standard deviation. For quantitative variables like gender, socio-economic status, educational status, opportunistic infection like pneumocystis Jiroveci, Pneumonia, cryptoccocal meningitis, cryptosporidiosis, cytomegalovirus retinitis, disseminated TB and toxoplasmosis were presented as percentages. Effect modifier like age, gender, duration of HIV, CD4 count, socioeconomic

status, and educational status were calculated through stratification. Post stratification chi square test was applied keeping p value < or equal to 0.05 as significant.

RESULTS: Total 154 patients of either gender with age above 18 years to 60 years meeting inclusion criteria of study were evaluated to determine the frequency of AIDS defining opportunistic infections in hospitalized HIV infected patients. Descriptive statistics were calculated using SPSS version 20. Stratification was done and post stratification Chi square test was applied to observe the effect of modifiers on outcome. P value ≤0.05 was considered as significant.

There were 71.4% male and 28.6% female patient. The overall mean age of patients was 39.56±7.76 years. The age was further stratified in two groups while the overall mean BMI was 20.61±3.88 kg/m2. The overall mean HIV duration was 15.25±5.09 months while the overall mean CD4 count was 174.17±12.85/cumm.

Among 154 patients, 40.3% were from lower class with monthly family income <15,000 PKR, 51.9% were from middle class with monthly family income between 15,000 PKR to 30,000 PKR and 7.8% were from upper class with monthly family income >30,000 PKR.

Among total study subjects, mostly got education till secondary level (49.4%)

In our study, 18.8% patient were found with disseminated tuberculosis, 31.2% with pneumocystis pneumonia, 12.3% with cerebral toxoplasmosis, 18.2% with cryptococcal meningitis, 3.9% with cryptospordiasis and 14.9% with cytomegalovirus retinitis.

The results showed that there was significant association of disseminated tuberculosis with gender (p=0.031) and age group (p=0.006). Cerebral toxoplasmosis was also found significant with educational status (p=0.006).

TABLE I: THE DEMOGRAPHICAL DISTRIBUTION OF THE STUDY POPULATION

GENDER	**FREQUENCY [n = 154 (%)]**
Male	110 (71.4)
Female	44 (28.6)
SOCIO ECONOMIC STATUS	
<15,000 PKR	62 (40.3)
15,000 to 30,000 PKR	80 (51.9)
>30,000 PKR	12 (7.8)
EDUCATIONAL STATUS	
Primary	55 (35.7)
Secondary	76 (49.4)
Inter	23 (14.9)

Table II: FREQUENCY DISTRIBUTION OF DISSEMINATED TUBERCULOSIS, PNEUMOCYSTIS PNEUMONIA, CEREBRAL TOXOPLASMOSIS, CRYPTOCOCCAL MENINGITIS, CRYPTOSPORDIASIS, CYTOMEGALOVIRUS RETINITIS (n=154)

	YES		NO	
	Frequency	**%**	**Frequency**	**%**
Disseminated TB	29	18.8	125	81.2
Pneumocystis pneumonia	48	31.2	106	68.8
Cerebral toxoplasmosis	19	12.3	135	87.7
Cryptococcal meningitis	28	18.2	126	81.8
Cryptospordiasis	6	3.9	148	96.1
Cytomegalovirus retinitis	23	14.9	131	85.1

DISCUSSION: It was not until recently that OIs became the leading cause of morbidity and death in this group. In the early 1990s, chemoprophylaxis and better OI management tactics increased patient quality of life and survival. 16 For those who live in countries where ART is available and inexpensive, the widespread use of ART beginning in the mid-1990s has had the greatest impact on lowering OI-related mortality.[16], [17], [18]

Given the existence of ART, OIs continue to cause significant morbidity and death. Many people are unaware they have HIV and seek medical attention when an OI appears. Some patients know they have HIV but refuse to take ART. Affiliation, pharmacokinetics, or other unexplained biologic variables may prevent certain individuals from achieving optimal virologic and immunologic response to ART. [19]

OIs are still the major cause of morbidity and mortality in HIV-infected people, even in countries where ART is widely available and inexpensive. Clinicians should know the epidemiology of these illnesses to give comprehensive high-quality treatment. These infections include bacteria, fungus, viruses, and protozoa. Often, they are reactivations of previous infections.

In a research by Balkhair AA, et al [20] 58 percent of HIV-positive patients had an AIDS-defining OI, and more than half had two or more. 77 percent of those with HIV had a CD4+ cell count of 200 cells/L or above. In India, 83.4% of patients were late.[21] In Europe, just one-third of patients were late HIV presenters.[22] Interesting discoveries. Whatever the underlying reasons, lowering late-stage HIV diagnoses by earlier and more widespread testing, and boosting early ART initiation and adherence would significantly decrease OI burden. In an Oman research, PCP accounted for 25% of all diagnosed OI episodes.[20] PCP was an AIDS-defining OI in 18 individuals (23%). Eleven individuals had PCP confirmed by microbes in induced sputum or BAL fluid. The remaining 7 patients had PCP. PCP prevalence in this group was greater than in Lebanon (10.9%) and considerably higher than in Europe (2–3% of PCP cases reported among HIV/AIDS patients).[23] In our study cohort, the reported percentage of patients diagnosed with PCP was 31.2%. Prior to the widespread use of primary PCP prevention and ART, 70–80% of AIDS patients had PCP. A research in Nepal found all instances in individuals with CD4+ levels under 200 cells/L.[24]

Oral candidiasis was the most frequent OI (59%) in the Omani HIV positive individuals group, comparable to Sharma S et al findings in Nepal.[24] Oral candidiasis is the second most prevalent illness among AIDS patients, according to some Indian researchers.[25], [26], [27] In Hong Kong144 and India, Mycobacterium TB was the most frequent isolate.[28] An Omani investigation found 35% pulmonary TB and 21% extrapulmonary TB.[20] In Brazil, pulmonary TB was the most frequent OI (52.9 percent).[29] People with latent M. tuberculosis infection are more likely to develop active TB.

In 2008, there were 1.5 million new instances of tuberculosis among HIV-infected people, and 26% of AIDS-related fatalities.[30] In the same year, 1.4 million TB patients were tested for HIV worldwide, with 81 nations testing over 50% of their TB patients. In the same year, just 4% of HIV-positive people were tested for TB.[31] TB is widespread in India and is the leading cause of mortality among AIDS patients.[32] Due to the high probability of reactivation of latent infection and sensitivity to new infection, HIV patients are more likely to acquire active TB.[33]

From 1985 to 1998, 173 HIV-infected individuals were studied in South Korea at an AIDS referral hospital to evaluate the prevalence and kinds of major opportunistic illnesses.[34]

Another research from Malaysia revealed CMV infection in 2% of their study sample of AlDS patients.[35] Luo B, et al. from Shanghai studied the percentage of admissions attributed to particular OIs among persons living with HIV (PLWH) and characterised the primary clinical

variables associated with each individual OI.[36] CMV was revealed to be the third most common OI, causing 20.9 percent of patients to suffer retinitis, viremia, pneumonia, and colitis.

In the prior research, just 3% of patients had Cryptosporidium infection.[35] while in Ethiopia, 21% of HIV patients had Cryptosporidium.[37] In this research, 3.9 percent of patients acquired cyrptosporidiosis. Enteric pathogen Cryptosporidium parvum causes gastroenteritis in humans. Cryptosporidiosis may induce deadly consequences such bile duct damage in HIV patients.[38] The use of ART has significantly reduced HIV/AIDS infection rates in several countries.[39]

Cryptococcus neoformans is the most common invasive fungus illness in HIV patients. Meningitis is the most prevalent symptom of invasive cryptococcosis in HIV patients. In an Arab research, Cryptococcus meningitis affected 22% of OI patients and 21% of HIV patients.[40] Cryptococcal infection (including meningitis) is about 6-8 percent in India, but it is 5-11 percent worldwide.[41] In this research, 18.2% of patients had cryptococcal meningitis. Strangely, none of the Lebanese patients had cryptococcal meningitis.[22]

Toxoplasmosis is an OI zoonotic disease Toxoplasma gondii. Immunocompetent people need serological testing for toxoplasmosis.[42] The incidence of dormant toxoplasmosis in HIV/AIDS ranges from 3-97 percent according on ethnicity.[43] Stroke is the leading cause of focal neurological problems in HIV patients. Balkhair AA et al [20] found that cerebral toxoplasmosis affected 12.5% of all AIDS-defining OIs and 12.5% of all HIV patients. In a Lebanon research, 21.9 percent of HIV-infected individuals had neurotoxoplasmosis.[22]

This substantial discrepancy likely reflects societal differences between the two communities. Toxoplasmosis-positive IgG, compatible brain lesions on CT/MRI, and detailed clinical response to toxoplasmosis treatment were all present in our cohort. Providing appropriate and sustainable antimicrobials, careful monitoring and follow-ups are key components of good OI diagnosis and treatment.[44] Poor treatment adherence is another possible risk factor for opportunistic infections while poor clinicopathologic state is associated with opportunistic infections whereas ART should be started early to minimise opportunistic infections by health authorities and physicians.[45], [46]

CONCLUSION: The study results showed pneumocystis pneumonia as the most prevalent infection followed by disseminated tuberculosis, cryptococcal meningitis, cytomegalovirus retinitis, cerebral toxoplasmosis, and cryptospordiasis. These findings showed the necessity of specific measures to prevent OIs. Clinicians and health planners can better combat the AIDS pandemic if they recognize and diagnose OIs in HIV patients. Early identification and treatment of OIs improves patient survival and delays the onset of AIDS.

Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Consent

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

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