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EPIDEMIOLOGICAL CHARACTERISTICS AND CLINICAL PRESENTATIONS OF HIV PATIENTS ATTENDING THE ABBASIA FEVER HOSPITAL

By

MOHAMED MOHEI EL BADRY[1], HAGAR A. ELESSAWY[2]*, And FATMA AHMED ALI-ELDEEN[3]

Department of Tropical Medicine and Gastroenterology, Aswan University[1], Department of Internal Medicine Gastroenterology Unit[2] and Department of Tropical Medicine[3], Faculty of Medicine, Ain Shams University[2,3], Cairo 11566, Egypt
(*Correspondence: doch_ain@hotmail.com)

Abstract

HIV/ADIS is one of uprising problem in Egypt as UNAIDS Estimated that more than 22 thousand people infected at the end of 2018 this represent less than 1% of population. Without screening in high risk groups and prompt management of infected patients this may lead to spreading of infection and death from opportunistic infections. The present study identified clinical presentations, characteristics of patients and risk factors associated with infection in positive HIV patients attended to Abassia Fever Hospital in a year (2015-2016). Data of clinical presentations and demographic characteristics of 100 consecutive patients were collected during admission. The results showed that 82% of patients were from urban area and 18% from rural area and 93% of patients were smoker (65%), married (80%) and were on regular HAART. Regarding clinical manifestations and CD4 count; 68% of the patients had ADIS criteria, 30% had diarrhea, 28% had chest infections, 59% had anemia and 64% had CD4 count less than 200cells/ µL however a single case had presented with Kaposi sarcoma.

Key words: Egypt, Abbasia fever hospital, HIV/ADIS, HIV clinical presentations.

Introduction

The human immunodeficiency virus (HIV) is a lentivirus (a subgroup of retrovirus) that causes the acquired immunodeficiency syndrome (AIDS) (Douek *et al,* 2009). From its discovery, almost 78 million people have been infected with the HIV and about 39 million people have died of HIV. An estimated 37.9 million people living with HIV at the end of 2018. Due to gaps in HIV services, 770 000 people died from HIV-related causes in 2018 and 1.7 million people were newly infected. Over two thirds of all people living with HIV live in the WHO African Region (25.7 million) (WHO, 2019). According to United Nations Program on HIV/ AIDS, there were 22.000 (20.000-24.000) people living with HIV/AIDS in Egypt by the end of 2018. An estimated 0.1% of adults aged 15-49 years are living with HIV. There were about 500 people died of AIDS-related illness in 2018 (UNAIDS, 2019). In 2018, for the first time, individuals from key population groups and their sexual partners accounted for over half of all new HIV infections globally (an estimated 54%) in 2018. For eastern European, central Asian, Middle Eastern and North African regions, these groups accounted for around 95% of new HIV infections. Key populations include men who have sex with men, people who inject drugs, people in prisons and other closed settings, sex workers and their clients, and transgender people (WHO, 2019).

There are four stages of HIV/AIDS for adults and adolescents with confirmed HIV infection defined by WHO and categories as clinical stage one that might be asymptomatic up to clinical stage four with severe form of opportunistic infections, this clinical stage was useful for assessment at baseline or entry into long-term HIV care and in the follow-up of patients in care and treatment program (WHO, 2007).

In the absence of specific treatment, about half of people infected with HIV will develop AIDS within ten years. The most common initial conditions that alert to the presence of AIDS are pneumocystis pneumonia (40%), cachexia in the form of HIV wasting

syndrome (20%) and esophageal candidiasis. Other common signs include recurring respiratory tract infections (Blankson, 2010).

Patients and Methods

Study area and period: The study was conducted in Abbasia Fevers Hospital, Cairo, among patients with proven HIV infection from February 2015 to February 2016, as a cross sectional observational study.

Study population: 100-consecutive patients recruited over one year with HIV-seropositive who attended to hospital during the period of February 2015 to February 2016.

All patients were subjected to: full history with emphasis on family member affection, intravenous drug abuse, sexual activity, previous blood transfusion, tattooing and previous surgical intervention.

HIV antibodies test by ELISA was done to confirm a reactive screening test; result a Western Blot (WB) analysis was typically carried out. It consisted of a set of nine HIV-specific bands (gp160, gp120, gp41, p66, p55, p51, p31, p24 & p17). When they were exposed to individual serum, the pattern of reactivity of these bands determined the HIV status. The method used for the scoring of the bands was the commercial kit. The WB kit used was weak positive control strip to score bands for each serum sample; any band stronger than the p24 band of weak positive control was scored as strong and those similar or weaker were scored as faint. Thus classify band reactivity in three categories was none, faint and strong.

Complications investigations: Full basic investigations were done and various samples (e.g. sputum, stool, urine, cerebrospinal fluids) were collected under universal aseptic precautions in suitable sterile universal containers. Specimens were stained using the Gram and Modified Ziehl-Neelsen stains and microscopically examined. Appropriate media were used for the isolation of pathogens which were further identified using standard protocols. Biopsy from skin or mucous membrane lesions, histopathological examination and gastrointestinal endoscopy were done when indicated.

CD4 count: Immunofluorescence analysis by flow cytometry is the gold standard for CD4 and T lymphocytes measurements. The flow cytometric works on the principle of scattering of light, granularity of the cells passing thorough the laser beam, and also by the fluorescence emitted by the cells after staining with the specific monoclonal antibodies to cell surface markers that were tagged with different fluorescence dyes. The population of interest was thus identified and gated for further analysis within the population of interest. The monoclonal antibodies specifically bind different surface receptors like CD4 for T helper cells. Relative percentages of the cells expressing the specific receptor on its surface are obtained from the flow cytometry and the absolute counts can be calculated with the help of absolute lymphocyte count.

Statistical analysis: IBM SPSS statistics (V. 23.0, IBM Corp., USA, 2015) was used. Data were expressed as Median and Percentiles for quantitative non-parametric measures and both number and percentage for categorized data. As categorized data; Chi-square test was used to study the association between each 2 variables or comparison between 2 independent groups. Probability of error at 0.05 was considered significant, but at 0.01 & 0.001 was highly significant.

Results

The study included 100 HIV patients; most of them were male; where male to female ratio was 4:1, with median age of 36 years (range 5-65 years). The majority of patients (65%) were married while 10 % were divorced and 20% were never married before. 25% of subjects were employed while 57% were manual worker and only 18% were unemployed. Most of patients were from urban area 82% while rural patients were 18% & 93 % of patients were smoker (Tab. 1).

Possible route of patient infection: Most of the patients had history of multiple sexual relations (76%) and the second most common suspected route was intravenous drug

abuse (71%) while family member affection was 53%. The least suspected routes' rates were tattooing 6%, blood transfusion 6% and surgical intervention 4% (Tab. 1)

The clinical stages of the study patients at presentation and according to WHO classifications; 64% of them were at AIDS stage. 36% were at the stage of clinical latency, however no one presented at the acute stage during the study period. Chronic diarrhea and bacterial urinary tract infection were the most reported manifestations in the studied patients (30% for each). The respiratory manifestations were in 28% of cases. Weight loss was present in 14% of HIV patients and 13% of them were accidentally discovered. Lymphadenopathy, esophageal candidiasis and septic meningitis were in 6%, 5% & 3% of cases respectively. Kaposi sarcoma was diagnosed in only 1% of the patients.

Laboratory examinations: CD 4 counts were < 200cells/µL in 64%, between 200 to 499cells/µL in 19% and above 500cells/µL in 17% (Tab. 2). Median hemoglobin was 9.8g/dl, Hb< 10 gm/dl was found in 59% of our studied population. Blood picture of 87% of the anemic patients in our study showed normocytic normochromic anemia, while 13% of anemic patient had microcytic hypochromic anemia. The mean total leukocyte count was 3500 cells/$mm^3$and the median of lymphocytic count (ALC) was 720 cells/mm^3. 80% of cases had absolute lymphocytic count less than 1500 cells/mm^3 (lymphopenia). Median of Absolute Neutrophilic Count (ANC) was 1365 cells/mm^3 and 69% of cases had Absolute Neutrophilic count (ANC) less than 2000 cells/mm^3. Mean platelet count was 78.5 and thrombocytopenia patients were 87% (Tab. 3).

Association between CD4 level and clinical presentations: There were statistically significant differences between CD4 level and diarrhea, chest infection, weight loss and lymphadenopathy (p = 0.0001, 0.005, 0.001 & 0.045 respectively) as with decrease of CD4 level than 200 cells per µL there were more cases that presented with diarrhea, chest infection, weight loss and lymphadenopathy, but all asymptomatic patient (13) had CD4 level more than 200 cells/µL. Also, the patient with Kaposi sarcoma had CD4 more than 200 cells/ µL, however all patient with esophageal candidiasis (5) and septic meningitis (3) had CD 4 level less than cells/µL (Tab. 4)

Table 1: demographics and risk factors of studied sample

Characteristics			Number/percentage
Gender	Male		80
	Female		20
Age	Median (range)		36 (5-65)
Residence	Urban		82
	Rural		18
Occupational status	Unemployed		18
	Employed		25
	manual worker		57
Marital status	Married		65
	Not married	single	20
		widow	5
		divorced	10
Regular use of HAART	Yes		80
Smoking	Yes	male	78
		female	15
Multiple Sexual relations			76
Intravenous drug abuse			71
Tattooing			6
Blood transfusion			6
Surgical intervention			4
Positive family history			53
Clinical latency			36
AIDS			64
CD4 Cell Count Categories	≥ 500		17
	200- 499		19
	< 200		64

Table 2: different clinical presentation of the studied sample

Clinical Presentation	Number/percentage
Chronic diarrhea	30
Chest infection	28
Weight loss	14
Asymptomatic (Accidentally discovered)	13
Lymphadenopathy	6
Esophageal candidiasis	5
Anemia	59
Bacterial urinary tract infection	30
Septic meningitis	3
Kaposi sarcoma	1

Table 3: different laboratory data of the studied sample

Parameters	Median		Number %	Institute reference values
Hb (gm/dl) range (5.5 – 13)	9.8	<10 gm/dl	59	12–18
		>10 gm/dl	41	
MCV (fl)	77.7	≥80 fl	92	80–96
		<80 fl	8	
MCH (pg/cell)	24.2	>27 pg/cell	92	27–32
		<27 pg/cell	8	
TLC cells/mm^3	3500	<4000 cells/mm^3	97	4000–11000 cells/mm^3
Absolute lymphocytic count (ALC) cells/mm^3	720	<1000 cells/mm^3	80	1500–3000 cells/mm^3 (20-45%)
Absolute Neutrophilic count (ANC) cells/mm^3	1365	<1500 cells/mm^3	69	2000 -7000 cells/mm3 (45-70%)
Platelets cells/mm^3	78500	<100 cells/mm^3	87	150.000-400.000 cells/mm^3
ALT	27			5-45u/l
Albumin	3.7			3-5gm/dl
Serum Total Proteins	6.4			6-8gm/dl
Creatinine	1.42			0.1-1.4mg/dl

Table 4: Relation between some clinical manifestations of patients and CD4 cell count

Clinical manifestations	No	CD4>200 cells per µL	Percent-age	CD4≤200 cells per µL	Percent-age	Pearson Chi-Square value	p-value
Chronic diarrhea	30	2	6.7	28	93.3	24.24	0.0001
Chest infection	28	6	21.4	22	78.6	8.04	0.005
weight loss	14	2	14.3	12	85.7	11.5	0.001
Asymptomatic (Acci-dentally discovered)	13	13	100	0	0	19.02	0.000
Lymphadenopathy	6	1	16.7	5	83.3	4.01	0.045
Esophageal candidiasis	5	0	0	5	100	6.7	0.010
Septic meningitis	3	0	0	3	3	2.43	0.119
Kaposi sarcoma	1	1	100	0	0	1.29	0.257

Discussion

The epidemiological aspects of HIV/AIDS in different geographical areas are important for the identification of behavioral and co-infectious factors, as these factors are associated with the spread and widely variable clinical course of the disease (Johnson *et al,* 2017). In Egypt, according to UNAIDS (2016), there are about 11,000 people currently living with HIV. Nevertheless, the unsafe behaviors among most-at-risk populations and limited condom usage among general population place Egypt at risk of a broader epidemic (Boutros and Skordis, 2010). Meanwhile, malaria was reported in Egypt (El Bahnasawy *et al,* 2010; Dahesh and Mostafa, 2015), there are interaction between malaria and HIV in non-pregnant women (Hewitt *et al,* 2006), also malignant malaria and HIV/AIDS are overlapping burdens in Africa (Saleh *et al,* 2019).

The present study described the demographic and clinical presentations of one hundred HIV patients attended to Abbasia Fever

Hospital during a period of one year. In the current study, the numbers of male patients (80%) were higher than females (20%) and the male to female ratio was 4:1. Male predominance was also observed (Celikbas *et al*, 2008; Avert, 2010). The male predominance might have been due to the fact that females do not seek medical care fearing ostracism and social stigma which decrease the number of females attending the HIV clinics. The low number of females may not be the true representation of the proportion of females. Nakama *et al.* (2015) documented higher prevalence of HIV/AIDS among females (68%) than among males (32%). Regarding the occupation of studied patients, 57% of subjects were manual workers. The present observations were similar to a study by Gupta (2009***)*** in Udupi where the most common source of income for HIV infected males (48.8%) was semi-skilled occupation. Majority of the subjects in the present study were from urban areas (82%), in contrast with a study conducted in South India by Chennaveerappa *et al.* (2011**)** who reported that 67% of the subjects were from rural areas**.** This observation could be due to the fact that Abbasia fever hospital is located in Cairo, the capital of Egypt with the maximum number of immigrant populations and visitors from worldwide. Of the HIV/AIDS patients 65% were married. This result agreed with Laah and Ayiwulu (2010) who found that this infectious disease was among married. This is worrisome because the high prevalence among those married has significant implication in the HIV/AIDS transmission. 93% of the patients were smokers. This result was higher than that reported by Tesoriero *et al*. (2010) who recorded a smoking rate of 59% among HIV patients in New York**.**

The commonest route of transmission was through multiple sexual relations (76%) followed by the intravenous drug abuse (71%). More heterosexual transmission rate was reported by Gupta *et al.* (2007). Pineda-Peña *et al.* (2018) reported that heterosexuals and homosexual was the most common route of infection 87.2% &1.1% for intravenous drug abuse. In the present study, many patients were reluctant to talk about their sexual life. But findings were not in accordance with Singh *et al.* (2007) who reported that intravenous drug abuse (53.7%) as the predominant mode of transmission. The present study showed that chronic diarrhea was the common manifestations in 30% of cases, while Moges and Kassa (2014) who studied the prevalence of opportunistic infection (OIs) in patient on anti-retroviral therapy (ART) showed that the commonest type of OIs among HIV patients in ART were oral candidiasis 50 (11.8%), followed by chronic diarrhea for greater than 1 month 42 (9.9%).

Kaposi sarcoma was histopathologically diagnosed in only 1% of patients. This result agreed with Kim *et al.* (2016) who reported 0.7%. However, the lower rate of HIV related cancers was justified by the small sample size studied. Septic meningitis was in 3% of patients, in form of Cryptococcus meningitis and septic meningitis. The present result agreed with Boniphace *et al.* (2011) who reported that Cryptococcus meningitis and Kaposi's sarcoma were diagnosed in only 3% of patients. The present study showed that in patients with advanced immunodeficiency with CD4 counts of less than 200 cells/µL infection of the esophagus was the cause of dysphagia. The commonest cause of esophageal symptoms was candidiasis, followed by cytomegalovirus infection which produced either diffuse esophagitis or discrete ulcerations (Wilcox and Saag, 2008). In the present study, weight loss was in 14% of HIV patients which was less than that reported by Ravikumar *et al.* (2010) they found that weight loss was in 34% of HIV patients. This difference may be due to the fact that their patients' samples suffered only from upper gastrointestinal symptoms. The incidence of HIV wasting syndrome has fallen dramatically in the era of successful antiviral therapy. However, weight loss and wasting still occur and associated with signi-

ficant morbidity and increased mortality.

In the present patients, the hemoglobin of 59% was <10gm/dl. Woldeamanue and Wondimu (2018) found that anemia was 41.9% of their patients before initiation of ART. Moges and Kassa (2014) also reported that HIV patients with a recent weight of less than 60 kg were 3.7 times more likely to develop OIs than their counter parts. In addition, current hemoglobin status was also another factor associated with of OIs. They found also that patients with hemoglobin level of greater than 10 mg/dl were less to develop OIs while, the patients with hemoglobin level of less than 10 mg/dl were 84% times more likely to develop OIs.

Anemia in HIV infection may be caused by HIV infection itself (most common), the bone marrow suppression by anti-retroviral therapy (Zidovudine is associated with macrocytic anemia), and opportunistic infection in AIDS. But, autoimmune hemolytic anemia was rare (Fauci and Lane, 2008). Anemia leads to decrease survival rate, rapid progression of disease and impairment of the quality of life. 150% more relative risk of death with baseline CD4 count <200 cells/μL in those with anemia than in those without (Lim and Levine, 2006).

In the present study, patients with thrombocytopenia were 87%. Thrombocytopenia was the most frequent cytopenia Lymphopenia (median level 750cells/mm^3) in 80% of cases and Neutropenia (median level 1365cells/mm^3) was in 69%. This agreed with Kasthuri *et al*. (2006).

In the present study, the number of thrombocytopenia patients were more compared to 5.9% reported by Wondimeneh *et al.* (2014). Many reports indicated a significant platelet sequestration and destruction in the spleen in HIV-associated thrombocytopenia. Platelet destruction occurred mostly in early course of the disease, while decreased platelet production predominantly occurred later. Antibodies directed against platelet glycoprotein IIIa were similar to those in classic ITP (Henry and Hoxie, 2005). Studies of the megakaryocytes from the HIV-infected patients showed viral RNA and proteins suggesting that these cells were infected in vivo (Coyle, 1997). Other studies showed that megakaryocytes express CD4 & CXCR4 were susceptible to HIV infection that led to thrombocytopenia include marrow infiltration by opportunistic infection or lymphoma, ITP, and myelosuppressive effects of drug therapy (Rozmyslowicz *et al.* 2003)

In the present study, among 30 cases with diarrhea the CD4 T cell count was less than 200 cells/μL in 28 cases (93.3%), while in 2 cases (6,7%) was more than 200 cells/μL. The CD4 counts were significantly lower in patients with diarrhea than those without (P =0.0001). Brink *et al.* (2002) correlated chronic diarrhea with CD4 T cell count found that diarrhea was positively related to less CD4 counts. Also, 13 asymptomatic HIV patients (accidentally discovered), all had CD4 T cell count more than 200 cells/μL.

In the present study, among 28 cases with chest infections CD4 T cell count was less than 200cells/μL in 22 (78.6%), but more than 200cells/μL in 6 (21.4%), with significant difference (P =0.005). Alan *et al.* (1998) found that once CD4 count dropped below 200cells/μL incidence of *Pneumocystis carinii* pneumonia, fungal pneumonia, and more severe forms of sinusitis, and bacterial pneumonia, including those caused by *Pseudomonas aeruginosa* rise dramatically.

In the present study, five patients with esophageal moniliasis had CD4 T cell count less than 200 cells/μL, with statistical significant (P = 0.010**).** This disagreed with many studies which reported that esophageal moniliasis occurred in any CD4 count from low to high **(**Barr, 1992; Vazquez, 2000; Bl\adon and Ross, 2007; Sanjar *et al,* 2011). Nevertheless, Kim *et al.* (2016) reported 16.2% of samples having candidiasis either oral or esophageal or respiratory all had CD4 less than 200cells/μl

Conclusion

The outcome data showed that the chronic diarrhea, urinary tract infection and chest

infection were the most common clinical presentations of the studied HIV patients while Kaposi sarcoma was only in one patient. Multiple sexual relations and intravenous drug abuse were the commonest risk factors found. Thus, the less the CD4 cell count (especially below 200 cells/μL) in the HIV patients the more was the associated the clinical manifestations.

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