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RESEARCH ARTICLE

OPPORTUNISTIC DIGESTIVE PARASITOSIS IN PATIENTS INFECTED WITH HUMAN IMMUNODEFICIENCY VIRUS IN MOROCCO

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Abstract

Introduction: Opportunistic intestinal parasites (OIP) are a major cause of diarrhea in patients with HIV infection. We carried out this study to assess the prevalence and characteristics of OIP in Marrakech.

Method: A retrospective cross-sectional study in a hospital environment was carried out in the infectious diseases department of Mohammed VI University Hospital, from January 2007 to October 2019. The diagnosis of OIP was made by parasitological examination of the stool, gastro panel intestinal FilmArray® multiplex PCR and / or histology.

Result: Forty-eight patients with IOP were included. The prevalence of IOP was 5.17%, 40 patients had cryptosporidiosis, 6 patients had microsporidiosis and 2 patients had isosporosis. Thirty patients had co-infection with other opportunistic infections. Thirty-five patients were on ARVs. Eleven patients (22.9%) died during the study and 77.1% did well.

Conclusion: The results of our study should prompt physicians treating HIV-infected patients in Morocco to request a stool exam and specific tests for *Cryptosporidium*, *microsporidia* and *Isospora*, especially in patients with low CD4 count.

Introduction:-

Diarrhea is a common complication of Human Immunodeficiency Virus (HIV) infection and occurring in almost 90% of AIDS patients in developing countries [2]. *Cryptosporidium*, *microsporidia*, and *Isospora belli* (also referred to as *Cystoisospora belli*) are the main opportunistic intestinal parasites (OIPs) agents, and are a well established cause of diarrhea among HIV infected patients worldwide, they can reduce both quality and duration of life, especially in those who are in contact with domestic animals, in area with contaminated water, and severely immunocompromised patients with CD4 T cell counts of <200cells/mm3 [5].

The prevalence of OIPs among HIV–infected individuals has dramatically decreased in countries where antiretroviral (ART) agents are widely available. However, in most African countries, opportunistic intestinal parasites still represent a frequent cause of diarrhea, weight loss, cachexia, and wasting [20]. The knowledge of the

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prevalence and characteristics of OIPs among HIV infected individuals would facilitate effective and control strategy programs intended to reduce the impact of these parasites amongst HIV patients [7]. To assess the prevalence of intestinal parasites in Marrakesh, we performed a cross-sectional study in HIV-infected adults followed in an urban center with a special focus on opportunistic protozoa.

Patients And Method:-

A hospital based cross-sectional retrospective study was conducted in the department of infectious diseases Mohammed VI University Hospital, Marrakesh, Morocco from January 2007 to October 2019. The Mohammed VI University Hospital is serving a large population. It provides different health services such as outpatients, inpatients, laboratory, medical imaging, pathology and pharmacy. The department of infectious diseases has been providing counseling and testing service for HIV since 2007. It also serves as a referral center for all other health institutions in Marrakesh Safi region. Screening as well as treatment and follow-up of HIV/AIDS patients is one of the routine services provided in the department.

We examined all cases of opportunistic intestinal parasitosis occurring in HIV-infected patients using medical records of the department of infectious diseases. The diagnosis of opportunistic intestinal parasites was made on parasitological stool examination, FilmArray® gastrointestinal panel multiplex PCR, and/or histology, and the following data were analyzed: age, gender, date of HIV infection, associated infections, CD4 cell count, plasma HIV RNA level, the use of antiretroviral (ART) agents, clinical presentation, presence and duration of diarrhea (defined as more than three loose or liquid stools in a 24 hours period) [7], presence of fever (temperature higher than 37.5°C), weight loss (kg), presence of other symptoms and treatment.

Also, as parasite shedding in stools is intermittent, patients are asked to deliver multiple stool samples for parasitic stool examination on three consecutive days [20].

Hence three stool samples from each patient were collected in sterile screw caped fecal containers and transported immediately to the laboratory. Epidemiological data were analyzed using Excel program version 2007 and Sphinx lexica, for data entry and statistical analysis.

Result:-

Prevalence and baseline characteristics

Forty-eight patients were diagnosed with opportunistic intestinal parasites and included in our study. The prevalence of OIPs in the present study was 5.17% (48/928 patients), various opportunistic intestinal parasites were found in the stools of our patients. The prevalence of *Cryptosporidium* was 4.31% (40 patients), followed by *microsporidia* 0.64% (6 patients), and *Isospora*0.21% (2 patients). *Cyclospora cayetanensis* was not detected in any of our patients. The confirmation methods of these parasites are listed in table I.

Out of 48 patients, 28 (58.3%) were males and 20 (41.7%) were females. The sex ratio (male: female) was 1.4:1. The mean age of patients was 34.4 years (range of 17-78 years). OIPs revealed HIV infection in forty-five patients (93.4%). The other patients had already been diagnosed with HIV infection.

Out of the 48 cases, CD4 T cell count data was available for only 46 patients (95.8%). The mean CD4 cell counts was 58cells/mm3. The majority (28 patients, 58.5% of 46) having CD4 counts of <50 cells /mm3, 7 (14.6%) had 51-100 cells/mm3, 9 patients (18.8%) had CD4 counts 101-200 cells/mm3, and 2 (4.1%) CD4 counts > 200 cells/mm3.

Clinical Manifestations

The clinical signs observed are listed in Table II. Asthenia and chronic diarrhea topped the list of symptoms shown in our patients, manifested by all patients (100%), followed by weight loss (44 patients, 91.8%), Deshydratation (30 patients, 62.5%), cough (18 patients, 37.5%), vomiting (14 patients, 29.2%), fever (13 patients, 27.1%), Dyspnea (12 patients, 25%) and abdominal pain (10 patients, 20.9%). The less common manifestations were neurological signs (7 cases), ophthalmological signs (3 cases), and skin signs (1 case).

Associated Infections

At the time of stool sampling, 30 (73.1 %) out of the 48 patients also had co-infection with others opportunistic

infections (OIs).The most commonly identified OIs recorded in these 30 HIV/AIDS patients were with esophageal candidiasis (18 cases, 37.5% of 48), followed by pulmonary or disseminated *Mycobacterium tuberculosis* infection (7, 14.6%), Non opportunistic intestinal protozoan (5, 10.4 %), *Cytomegalovirus (CMV)* infection, cerebral toxoplasmosis (4 each, 8.3%), *pneumocystis jirovecii* pneumonia (3 , 6.25%), *cryptococcosis*, syphilis (2 each, 4.1%), *listeria* bacteraemia and *hepatitis C* infection (1 each, 2.1%). (Table III)

Treatment And Outcome

Supportive treatment was based on rehydration therapy, electrolyte replacement, antimotility agents and parenteral nutrition.

Patients who had cryptosporidiosis received treatment with Azithromycine 500mg od for 3 weeks, and patients who had microsporidiosis received treatment with Albendazole 400mg bid for 3 weeks, and patients who had isosporiasis received treatment with cotrimoxazole at a median dose of 3200 mg tid for 10 days.

In addition, there were 35 (72.9% out of 48) patients who were on ART agents and 13 (27.1 %) who were not, due to reasons such as late presentation, side effects, and noncompliance.

Thirty seven patients (77.1%) have done well and 11 patients (22.9%) died during the study (7 had cryptosporidiosis, 2 had microsporidiosis, and 2 had isosporiasis). The cause of death was complications of diarrhea and ionic disorder in 6 patients and co infection with other OIs in 5 patients.

Discussion:-

Our study focused mainly on opportunistic protozoa, a frequent cause of chronic diarrhea and wasting in HIV-infected patients in African developing countries. To our knowledge, the present study is the first study that evaluates the prevalence of OIPs among HIV infected individuals in Marrakesh. In addition it is one of rare population-based prevalence study worldwide to determine the exact prevalence of OIPs, since it was based on the follow up of all 928 patients followed at our department, and included all cases of opportunistic intestinal parasitosis occurring in these patients over 12 years period, which was not available for many other studies [29].

Cryptosporidium parvum, *microsporidia*, and *I. belli* accounted for the most of OIPs, their diagnosis is difficult because of the special staining methods required [12,24,28].

The prevalence of OIPs in HIV patients varies according to studies, depending on age of the patients, where they were conducted, the stage of disease (HIV/AIDS), the laboratory methods, and the presence or absence of symptoms [6,7,9]. The overall prevalence of OIPs in the present study was 5.17%. This prevalence was consistent with those found by Badaoui et al and Soli et al (4 and 6.2% respectively) [1,8], but other studies reported higher prevalence [17]. (Tableau IV)

In the present study, all patients were symptomatic. Data from other studies show that OIPs might occur in both symptomatic and asymptomatic patients [7,23]. And the inclusion or not of asymptomatic patients can be an important factor that explain the disparity of prevalence among studies.

The male predominance in this study (sex ratio 1.4:1) has previously been described in many other studies [7, 8, 16, 21]. However, one study conducted in Nepal suggested that females had higher chance of OIPs than males [13], this difference can be due to ecological, environmental, economic and cultural factors that influence exposure to infection and risk of disease [25].

Cryptosporidium spp was the most prevalent and known causative agent for the majority of diarrhea and enteritis among OIPs [7,16]. Its prevalence was consistent (4.31%), with the result found by Sangaré et al (5.2%) [26], higher than the findings of Badaoui et al (2.4%) [8]. However, it was very lower than the findings of Kulkarni et al (12%) [17]. This difference might be due to variations in diagnostic approaches, sample size, and treatment to prevent OIPs in HIV patients. The second most prevalent OIP was microsporidia (0.64%). Its prevalence was low as compared to findings of Kulkarni et al (1%), Badaoui et al (2%) and Waywa et al (9.7%) [8,17,30]. However, it was consistent with reports fromFrance (0.8%) and India (0.7%) (18,19). Finally the prevalence of *Isospora belli* observed in this study was very low (0.21%) which was consistent with the findings of Badaoui et al (0.28%) [8] , but was far lower compared to other studies conducted in India (8%) and sub-Saharan Africa (1.3 to 24.3%)

[17,29]. We have not found *Cyclospora cayetanensis* in our patients, this parasite is very rare and it has not be isolated inother reports [23].However, in many studies this protozoan infection was identified and its prevalence range from 5 to 31% [17,29].

The clinical characteristics of patients with opportunistic intestinal parasites in this study were very similar to those of previously published studies. In our series, asthenia and chronic diarrhea were the most common symptoms, which goes in line with a similar study conducted in Congo [21] like other published studies [11] fever was common among our patients. Pulmonary manifestations (cough 37.5% and Dyspnea 25%), seemed quite frequent in our study, this could be explained by the pulmonary localization of cryptosporidiosis who was confirmed in 5 patients and suspected in 2 patients. This localization can occur in association with intestinal localization and be responsible for pulmonary symptoms [27].

Opportunistic infections (OIs) are found frequently in HIV positive patients, especially when the CD4 T-cell count is less than 200 cells/ µl [4]. In this study, 95.8% of patients had CD4 T-cell count <200 cells/ µl, and 73.2% of our patients were co- infected mainly by other OIs. Previous study highlighted that OIPs infected patients, especially if CD4 cells count <50 cells/mm3, were infected with many other OIs, because severely immunocompromised patients tend to be more susceptible to infections [10]. Of note, 58.5% of our patients had CD4 counts <50 cells/ mm3, and 95.8% had CD4 counts cells <200 cells/mm3. Our profile of OI coinfections were similar to that of Iqbal et al [7]. Esophageal candidiasis and tuberculosis were the most common co infection in the present study, the same result was found in India and Mozambique [15,22] however in Nepal [14], Toxoplasmosis was more common.

Following the introduction of ART agents, the prevalence of opportunistic infections and especially those of protozoal intestinal infections has dramatically decreased [20], in this study 72.9% of patients were on ART agents, and the prevalence of OIPs was 5.17%.

The majority of our patients have done well. The mortality rate in our series was 22.9%. These results were similar to those of Badaoui et al (19%) [8], butlower than the findings of NELSON et al (42%) [3] and Konate et al.(57%) [16]. This can be explained by the early and adequate management of our patients.

Conclusion:-

In this study of 48 HIV infected adults with opportunistic intestinal parasites in Marrakesh, the prevalence of intestinal parasites was 5.17%. The results of our study should therefore prompt physicians caring for HIV-infected patients in Morocco to request stool examination and specific tests for *Cryptosporidium*, *microsporidia*, and *Isospora*, especially in patients with low CD4 cell counts. However parasitic stool examinations should be performed in HIV infected patients with diarrhea even if the CD4 count is above 100 cells/mm3.

However, further studies evaluating the prevalence of OIPs at a national scale are needed to support these findings.

Table I:- Methods of diagnosis for each opportunistic intestinal parasites.

	Cryptosporidiosis	Microsporidiosis	Isosporiasis
parasitologicalStoolexamination	40	6	2
Filmarray	4	--	--
Histology	2	--	--
Sputumparasitologicalexamination	5	--	--

Table II:- clinical signs.

			Number of patients	**percentage**
General signs	**Asthenia**		**48**	**100%**
	Weight loss		**44**	**91.8%**
	Fever		**13**	**27.1%**
	Dehydratation		**30**	**62.5%**
		plan A	20	41.7%
		plan B	7	14.6%

		plan C	2	4.2%
Gastro intestinal symptoms	**Diarrhea**		**48**	**100%**
		Watery	38	79.2%
		Mucous	7	14,6%
		Bloody	3	6.3%
	Abdominal pain		**10**	**20.9%**
		Diffuse	6	12,5%
		Epigastric and right upper quadrant	4	8.3%
	Vomiting		**14**	**29,2%**
		of food	11	23%
		Bilious	3	6.3%
Respiratory signs	**Cough**		**18**	**37.5%**
		Productive	12	24,9%
		Dry	6	12,5%
	Dyspnea		**12**	**25%**
	Chest pain		**1**	**2,1%**
Other signs				
	Neurological signs		**7**	**14,6%**
	Skin signs		**1**	**2,1%**
	Ophthalmological signs		**3**	**6.3%**

Table III:- Opportunistic and non opportunistic associated infections.

Opportunistic infections			N	%
	Esophagealcandidiasis		**18**	**37.5**
	Tuberculosis		**7**	**14.6**
		Disseminated	4	8.3
		Pulmonary	3	6.25
	Toxoplasmosis		**4**	**8.3**
	Cytomegalovirus (CMV)		**4**	**8.3**
		Retinitis	3	6.25
		Viraemia	1	2.1
	Pnemocystispneumonia		**3**	**6.25**
	Cryptococcosis		**2**	**4.1**
Non opportunistic infections	**Intestinal protozoan**		**5**	**10.4**
		Amoebiasis	3	6.25
		Giardiasis	2	4.1
	Primary syphilis		**2**	**4.1**
	Hepatitis C		**1**	**2.1**
	Listeria bacteraemia		**1**	**2.1**

Table IV:- Prevalence of opportunistic intestinal parasites compared to other studies.

Study	Country	Prevalence
Soli J et al	Niger	6.2%
Kulkarni SV et al	India	35%
Badaoui L et al	Casablanca/ Morocco	4%
Our study	Marrakesh/Morocco	5.17%

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Conflicts of Interest
None.

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