

SPECTRUM OF OPPORTUNISTIC INFECTIONS IN AIDS CASES IN A TERTIARY CARE HOSPITAL IN NEPAL

Hari Shanker Joshi*, Rabindranath Das**, Arun Kumar Agnihotri**,

Sonu H. Subba**, Ramnesh Murthy**, S.B. Dabral***

Lecturer*, Assistant Professor**, Professor and Head***

Manipal College of Medical Sciences & Manipal Teaching Hospital, Pokhara Nepal and
M.L.N. Medical College, Allahabad

Abstract :

A retrospective study was carried out, 404 clinically suspected cases attending AIDS clinic at Manipal Teaching Hospital, Pokhara, Nepal to assess an occurrence of opportunistic infections in AIDS cases. Study reveals that Tuberculosis (60%), Cryptosporidiosis (13.33%) and candidiasis (11.11%) are the predominant opportunistic infection in HIV/AIDS patients in the Pokhara village. Next common pathogen was found an ubiquitous yeast, candida obtained from skin, oral cavity, oesophagus, sputum and stool. The least common documented documented infection was pneumocystis carini pneumonia (2.22%).

KEY WORDS : HIV, Opportunistic infections, Tuberculosis, Cryptosporidium, Candida.

Introduction :

The emergence and subsequent pandemic spread of acquired immuno-deficiency syndrome (AIDS), caused by the retrovirus, human immunodeficiency virus (HIV) is posing and enormous challenge to public health in modern times¹. In South-East Asia, the number of reported cases continue to increase alarmingly, imposing new demands on health care systems². The UN General Assembly-2001 has estimated 20 million deaths due to AIDS throughout the world by 2001. The first case of AIDS in Nepal was reported in 1988³. The National Center for AIDS and STD Control (NCASC) had formulated a policy requiring all cases of HIV/AIDS to be reported to its center at Katmandu. Opportunistic infections caused by the devastation of the host immune system by HIV are the major cause of morbidity and mortality in AIDS cases. These organisms are responsible for easily treatable

infections in immunocompetent patients. Despite observing an increasing trend in the reported HIV/AIDS cases in Nepal, the actual spectrum of opportunistic pathogens is not very clear. There is no available database of the commonly occurring opportunistic pathogens with a view to regional distribution in this country. The aim of the present study was to identify the commonly occurring opportunistic pathogens recovered from the clinical specimens and to initiate early diagnosis and treatment so as to reduce to morbidity of the AIDS cases.

Materials & Methods :

- A. Study group: A retrospective analysis was done of 404 clinically suspected cases attending AIDS clinic at Manipal Teaching Hospital, Pokhara, Nepal, during the time period from July 2001 to December 2002.

All the patients belonged to different municipality wards (total 18 wards) of Pokhara city and maximum cases were referral from local physicians. The patients were investigated for various infectious agents including those causing opportunistic infections.

B. Detection of HIV infection : HIV infection in patients were confirmed according to WHO strategy II, (1993), when at least two of the following tests were positive: HIV1 & 2 (Tri Dot ELISA , J Mitra & Co Ltd, New Delhi, India) HIV-Spot (Eli scan, Ranbaxy, New Delhi) and HIV 1 & 2 Western Blot (Gene Lab Diagnostics, Singapore) Before screening, an informed consent taken and pretest counseling was done in all suspected cases (total 404).

C. Collection and Processing of clinical

specimens: Various representative specimens e.g, sputum, CSF, blood, urine, stool, bronchoalveolar lavage, oesophageal brushings and lymph node aspirate were collected as per clinical presentations. They were transported in universal container to the Department of Microbiology and were processed for different pathogens in safety cabinet using stringent precautions. Lowenstein jensen media and Sabroud's dextrose agar media were used for isolation of Mycobacterium and Candida respectively following standard procedures. Following staining methods e. g., Gram's, Giemsa, Ziehl Nielsen, Auramine phenol technique, modified cold Ziehl Nielsen stain were used and microscopical examinations were carried out including wet mount preparation and formal ether concentration technique for stool were used in the present study^{4,5}.

Result :

TABLE - I
Distribution of HIV Positivity according to age and sex

Age group	HIV positive			HIV negatibe			Total
	Male	Female	Total(%)	Male	female	Total	
<19	03	02	05 (6.76)	06	05	11	16 (3.96)
20-39	47	08	55 (74.32)	72	94	166	221 (54.70)
40-59	07	04	11 (14.87)	74	30	104	115 (28.47)
>60	02	01	03(4.05)	31	18	49	52 (12.87)
Total	59	15	74(100)	183	147	330	404 (100)
	79.73)	(20.27)	(18.32)			(81.68)	(100)

$\chi^2 = 19.52, p < 0.001$, Odds Ratio = 3.16, Confidence interval (C¹) = 1.66-6.08

Table I shows that out of 404 suspected cases, 74 (18.32%) detected HIV Positive, in which maximum 55 (74.32%) were in the age group of 20-39 year. 59 (79.73%) of HIV positive were males and 15 (20.27%) were females.

The odds ratio calculated for HIV positivity and sex was 3.16 with confidence interval 1.66-6.08 and $p < 0.001$, shows strong association between HIV positivity and sex.

TABLE - II

Distribution of HIV Positivity according to literacy status

Literacy status	HIV Test		Total (%)
	positive	Negative	
Illiterate	21(28.38)	198	219(54.21)
Primary	41(55.41)	96	137(33.91)
Secondary & above	12(16.21)	36	48(11.88)
Total	74(100)	330	404(100)

$X^2 = 24.93, p = <0.001$

In Table II, out of 404, 219 (54.21%) cases were illiterate. The proportion of illiterate among HIV positive cases found to be 28.59%

and proportion of cases with primary level education was 55.41%. Association between literacy and HIV positivity was found to be significant ($x^2=24.93, p=<0.001$).

TABLE - III

Distribution of the factors influencing modes of transmission of HIV

Factors	HIV Test		Total(%)
	Positive	Negative	
Sex workers or clients of sex workers	45 (60.81)	103	148 (36.63)
Blood product Recipients	1 (1.35)	22	23 (5.69)
IVDUs	16 (21.63)	113	129 (31.93)
House Wives	09 (12.16)	84	93 (23.03)
Mother to child	03 (4.05)	08	11 (2.72)
Total	74(100)	330	404(100)

$x^2 = 25.70, p = <0.001$

In Table III the proportion of sex workers or clients of sex workers in HIV positive cases were found to be 60.81% and the proportion of IVDUs was 21.63%. Proportion of vertical trans-

mission from infected mother to the baby was found to be 4.05%. Association between factors responsible for transmission and HIV positivity was found to be significant ($x^2=25.70, p=<0.001$).

TABLE - IV
Clinical spectrum of 74 patients with HIV infection

Clinical symptoms	HIV Positive (N=74)
Fever	36(48.65%)
Weight loss	27(36.49%)
Cough & dyspnoea	27(36.49%)
Dysphagia	19(25.6%)
Chronic Diarrhea	12(16.22%)
Generalized Lymphadenopathy	14(18.92%)
Meningitis	7(9.46%)

Table IV shows that the commonest presenting clinical symptom in HIV positive cases was fever (36;48.65%) followed by weight loss (27;36.49%), cough and dyspnoea (27;36.49%)

Proportion of chronic and recurrent diarrhoea was found in 16.22% cases. Proportion of Meningitis was found to be 9.46%.

TABLE - V
Distribution of pathogens detected in HIV infected patients (n=45)

Organisms	Specimens	No of Isolates	percentage
Mycobacterium tuberculosis	Sputum	16	60.0
	Lymph node	07	
	CSF	04	
	Total -	27	
Cryptosporidium species	Stool	06	13.33
Candida albicans	Esophageal brush	05	11.11
Cryptococcus neoformans	CSF	03	6.67
Isospora belli	Stool	01	2.22
Pneumocystis carinii	BAL Full form	01	2.22
Strongyloides stercoralis	Stool	01	2.22
Cyclospora species	Stool	01	2.22
Total organisms		45	100

Table-V shows the distribution of infectious agents in the different types of clinical specimens obtained from the patients in this study.

Among the pathogens detected, Mycobacterium tuberculosis was the most common pathogen (27/45; 60%) followed by Cryptosporidium species (6/45;13.33%) The

third commonest pathogen was candida species (5/45; 11.11%) followed by cryptococcus neoformans (3/45; 6.67%). Cyclospora species (1/45; 2.22%), Strongyloides stercoralis (1/45; 2.22%), Isospora belli (1/45; 2.22%) and Pneumocystis carinii (1/45; 2.22%), one each was isolated from different patients.

Discussion :

High mobility of the young and adult Nepali citizens in search of jobs to neighboring countries and subsequent promiscuous behavior, low level of knowledge of HIV/AIDS and its preventions were some of the discernible factors for increased prevalence of HIV/AIDS in Nepal. These findings are consistent with other reports from Nepal and bordering Indian states^{6,7}

Candidiasis (11.11%), dermal or mucosal, oral and oesophageal was very common infection in the present study. It had been recognized as a common infection among HIV infected persons who form an important group to be screened for HIV infection.⁸

In our study, we found that Mycobacterium tuberculosis was the commonest infection in the HIV infected patients (60%) followed by Cryptosporidiosis (13.33%) and candidiasis (11.11%)

Tuberculosis clearly emerged as the major public health problem. Studies in the USA, African countries and neighboring country like India have also shown similar findings^{8,9}. The reported annual incidence rate of tuberculosis is more than 1% and an estimated 2% of total population has active tuberculosis in Nepal. With an estimated population of 23.2 million (2001 Census) in Nepal, tuberculosis threatens to spread at an alarming pace. "HIV-TB Link" has a devastating impact in the developing world where 95% of the people living with dual Tuberculosis and

HIV infection. HIV infected people have a six to thirty times greater risk of developing tuberculosis compared with people not infected with HIV¹⁵.

Pulmonary tuberculosis was present in 35.55% (16/45%) while mycobacterium tuberculosis was isolated from lymph node and CSF as extra-pulmonary tuberculosis in 24.44%; (11/45). Some of these findings agree and other disagrees with other published studies in Nepal and abroad¹². Cryptosporidium related diarrhoea was found to be the second most common infection (6/45; 13.33%) It cause occasionally acute profuse watery diarrhea in children, which are self-limiting, but in immuno-compromised patients like AIDS it can cause chronic diarrhea. Prevalence of Cryptosporidiosis in Nepal is not known. Laboratory rates of detection of Cryptosporidium oocyst in nonimmuno-compromised subjects average about 2% in developed countries and 8% (range 2-30%) in developing countries¹⁴. It is well recognized that most of the morbidity and mortality of late AIDS is associated with gastrointestinal disease. Cryptosporidium, Microsporidia, Cyclospora - these Protozoa are responsible for severe malabsorption, maldigestion and chronic diarrhoea - which leads to massive weight loss and ultimately succumb to death.

Similar study in Thailand, during Jan. 1994 to June 1997 among 91 HIV infected patients with chronic diarrhoea brought out that microsporidia and Cryptosporidium parvum were the most common parasites in HIV infected patients and were significantly more prevalent than in non-HIV Infected cases (29% vs 0% for microsporidia, $p < 0.001$ and 25% vs. 1% for c. parvum, $p < 0.001$)¹⁶.

In our present study, meningitis due to Cryptococcus neoformans occurred in 3 patients (6.67%). This true yeast finds a suitable medium for growth in the

subarachnoid space as compared to toxoplasma carried by hematogenous route lodge in the grey matter of diencephalons. This Neurological complication of Cryptococcus meningitis is highlighted because it is known to cause considerable morbidity and high mortality. Moreover, it interferes with the physical capability to perform one's own daily activities in the late stage of the disease.

In Senegal, similar study had done on 980 HIV infected patients in which total 7 (6 men & 1 women) Cryptococcus meningitis cases were found¹⁷.

Isospora associated diarrhoea was observed in 1(2.22%) patients, which is less than the 21% prevalence reported from an Indian study¹⁰. In studies in Haiti and Los Angeles, USA the prevalence was reported to be 15% and less than 1% respectively¹¹.

Isospora belli, Cyclospora and Strongyloides stercoralis associated diarrhoea were detected in 3 patients (6.66%). Other pathogen namely Pneumocystis carinii associated pneumonia was seen in only one case (2.22%) Prevalence of these pathogens in HIV patients in variable as per published reports^{10,13}.

The present study documents that tuberculosis, cryptosporidiosis and candidiasis are the most predominant opportunistic infections in the HIV infected patients in the Pokhara valley (Western Development Region) of Nepal. To the best of our knowledge, it is the first study of its kind in the region highlighting the variety of opportunistic infections in HIV patients. Due to the ever so changing pattern of infection, timely diagnosis and intervention and constant monitoring of magnitude of the HIV infection is necessary for better patient care and management. Further studies involving different regions of Nepal with inclusion of greater number of HIV

patients and an accurate analysis of various spectrums of opportunistic infections in HIV/AIDS patients would help in establishing the epidemiological database of these commonly occurring opportunistic infections.

Conclusion :

The present study mainly emphasized the opportunistic infection commonly observed in immuno-compromised HIV/AIDS cases. In a developing nation like Nepal where anti-retroviral treatment is almost not feasible owing to non-availability and economic constraints, we aimed to treat the symptomatic opportunistic infection only. Mycobacterium tuberculosis was found to be the most common opportunistic infection. Second common opportunistic pathogen was Cryptosporidium induced chronic diarrhoea and malabsorption, which was due to lack of sanitary control of food and water, personal hygiene and proper disposal of excreta. The next most common pathogen was the ubiquitous yeast, Candida obtained from skin, oral cavity, oesophagus, sputum and stool. The least common isolated documented in this study were pneumocystis carinii pneumonia. As the present study, is a small retrospective analysis of patients attending the AIDS clinic at our hospital, long-term studies involving a larger population are required to draw a conclusion of the epidemiological significance of these opportunistic infections.

Secondly, this study highlights the importance of instituting early symptomatic treatment of opportunistic infections of AIDS cases, which will definitely reduce the morbidity of those patients.

Though this small article is intended for drawing the attention of policymakers, health administrators, doctors, nurses, and care providers it also deserves attention of widest possible readers from rich countries of

Middle-east and Western world.

References :

1. World Health Organization: The Current Global Situation of HIV /AIDS pandemic. *Wkly Epidemiol Res* 1993, 68: 195-6.
2. Who 1999: Health Situation in the South-East Asia Region 1994-1997, Regional Office for SEAR New Delhi.
3. Subedi B K Presentation of AIDS in Nepal. *J Inst Med* 1998;20 (1,2): 53-57.
4. Baron EJ, Finegold SM. Baily and Scott's Diagnostic Microbiology, 8th edn Mosby: St Louis,1990.
5. Gradon J D, Timpone J G and Schnitman SM. Emergence of Unusual Opportunistic pathogen in AIDS; a review. *Clin Infect Dis* 1992, 15: 134-57.
6. Subedi B K. Gurubacharya V L. Sexual behaviour pattern in Nepal *J Inst Med*, 1994; 14:198-204.
7. Ayyagiri A, Sharma A K, Prasad K N, Dhole T N, Kishore J and Chowdhary G: spectrum of opportunistic G I pathogens in AIDS patients. *Ind J Med Microbiol* 1999, 17 (2): 78-80.
8. Kumaraswamy N and Soloman S et al. Spectrum of opportunistic infections among AIDS patients in Tamil Nadu, India. *Int J STD AIDS* 1995; 6: 447-9.
9. Lopez Dupla and Mora Sanz Pet: Clinical, edoscopic, immunological and therapeutic aspects of oropharyngeal and oesophageal candidiasis in HIV infected patients; a survey of 114 cases. *Am J Gastroenterol* 1992; 87: 1771-76.
10. Sorvillo F J, Lieb L E, Siedel J: Epidemiology of Isosporiasis among patients with acquired immunodeficiency syndrome in Los Angeles County. *Am J Trop Hyg Med* 1995; 53: 656-9.
11. Prasad K N: Gastroenteritis in immuno-compromised host. In proceeding of "Curreny concept of microbial infectio in immuno-compromised host" of Iono- US CME, Prasad K. N. and Ayyagiri A (ed) Department of Microbiology, SGPGIMS, Lucknow, 1996: 43-45.
12. Sharma SK. Pandey JN: HIV infection and tuberculosis. *Ind J Chest Dis Aied Sci* 1994; 36:109-11.
13. Lanjeswar D. N. Rodrigueuz C: Cryptosporidium, Isospora and Strongyloides in AIDS. *N. Med J. Ind*, 1996:17-19.
14. Casemore D.P. Roberts C. Guidelines for screening for cryptosporidium in stool: Report of a joint working group: *Journal of clinical pathology*, 46, 2-4.
15. Rarigliion MC et al. HIV Associated Tuberculosis In Developing Countries, Clinical Features Diagnosis And Treatment, *Bulletin Of The World Health Organization*, 1992 (2) 70.
16. Sow P.S., Diop B M, Dieng Y et. al. Cryptococcus Meningitis And HIV Infection In Darker Maladies Infection, 1998. (6-7) 511-515.
17. Wanchiwanawin D. Manasathi. S. et. al. Intestinal Parasitic Infections In HIV and Non HIV Infected Patients in Chronic Diarrhoea In Thailand, *Siriraj Hospital Garrette* 1999, 51 (3) 147-152, Department Of Parasitology, Siriraj Hospital, Mahidol University, Bangkok.
