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OPPORTUNISTIC INFECTIONS AND CLINICO-EPIDEMIOLOGICAL FACTORS IN HIV/AIDS CASES SEEN IN A TERTIARY CARE HOSPITAL IN NEPAL

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Opportunistic infections are the leading cause of morbidity and mortality among HIV/AIDS patients. The spectrum of opportunistic pathogens involved in such infections in Nepal is not well documented. A cross sectional (hospital-based) study was carried out at the AIDS clinic of Manipal Teaching Hospital, Pokhara, Nepal. A total of 404 clinically suspected cases of HIV/AIDS seen at the clinic between July 2001 and December 2002, were screened for HIV. Seventy four (18.3%) were sero-positive for HIV. Fever was the commonest presenting symptoms 48.6% followed by cough and dyspnoea 36.5%, weight loss 36.5% and pulmonary tuberculosis 21.6%. Fifty five of the 74 (74.3%) HIV positive cases were in the age group 20-39 years. Heterosexual mode of acquisition/transmission was seen in 60.8% and 21.6% were intravenous drug abusers (IVDA). A total of 45 opportunistic pathogenic isolates were recovered from the 74 patients. *Mycobacterium tuberculosis* was the commonest pathogen 60%, followed by *Cryptosporidium spp* 13.3% and *Candida spp* 11.1%. Four patients died during the period of study giving a mortality rate of 5.4%. This study shows that HIV/AIDS is rapidly becoming a grave concern in the Pokhara valley of Nepal. Intensive and effective health education programmes among the target population may be a cost effective method to curb the rising prevalence of HIV/AIDS in a developing country like Nepal. Also, further regional studies are required to establish more detailed epidemiological database of opportunistic infections in HIV/AIDS patients in Nepal.

Keywords: HIV/AIDS, Opportunistic infections, Nepal

INTRODUCTION

Human Immunodeficiency Virus (HIV) is the most significant emerging infectious pathogen of the 20th century (1). HIV infection leading to acquired immunodeficiency syndrome (AIDS) is probably the most crucial issue with regard to its economic, cultural and social impact in the population worldwide. Since its recognition in 1981, it has reached pandemic proportions affecting the whole world (2).

In South-East Asia, about 216, 443 AIDS cases have been reported up to March 2002 and over 90% of them were reported after 1993 (3). Also, the estimated population living with HIV infection up till March 2002 was about 5.3 million (4). In 2000, the prevalence rate of HIV/AIDS infection in South-East Asia was more than 358 per 100,000 populations (5). HIV/AIDS was the leading cause of death in the age range 15-49 years in South-East Asia in 1998 and the number of all STD cases excluding HIV/AIDS was 3, 107, 007 (5). According to the latest reports published in June 2002, there are nearly 3.86 million HIV sero-positive cases and 39,742 full-blown AIDS cases in India (5).

The first reported case in Nepal was in July 1988 (6). A growing trend has been observed in the number of reported HIV/AIDS cases after 1998 (7). According to the National Centre for AIDS and STD Control of Nepal (NCASC), established in 1986, seropositivity among voluntarily tested individuals in 1997 was 3.58% and this figure increased to 6.1% in December 1998 (8). The number of HIV infected persons in Nepal, as of June 1999, was 25,000 with a prevalence of 66 per 100,000 populations (3). The estimated number of cases up to 2002 was about 34, 000 and the expected number of deaths from AIDS in year 2002 is close to 3, 000 and this figure is projected to more than double in 2005 (9).

This exponential growth rate of HIV/AIDS in the recent years in Nepal can

be attributed to increasing number of new HIV/AIDS infection, more awareness of the disease and availability of serological and diagnostic tools for testing (10). Despite observing an increasing trend in the reported HIV/AIDS cases, the spectrum of opportunistic infections in these patients is not well documented. Also, there are no available epidemiological data on the regional distribution of these opportunistic infections in the country.

In an effort to document the clinical and the epidemiological profiles of the disease, a study was undertaken at Manipal Teaching Hospital (MTH), Pokhara, Western Development Region, Nepal to determine the proportion of seropositivity in clinically suspected cases of HIV/AIDS; to evaluate the spectrum of clinical presentations of HIV/AIDS cases; to determine the epidemiological factors responsible for transmission of HIV/AIDS and to identify the commonly occurring opportunistic pathogens associated with HIV infection. This knowledge will serve as guides in the antimicrobial therapy of opportunistic infections in HIV/AIDS patients and in formulating control measures to reduce transmission of HIV in Nepal.

MATERIALS AND METHOD

Study design/area

A hospital based cross-sectional study was conducted in HIV/AIDS clinic at Manipal Teaching Hospital, Pokhara, Western Region, Nepal, during the period July 2001 and December 2002. Manipal Teaching Hospital is a tertiary care center located in Pokhara sub metropolitan with the population of about 1.79 hundred thousand (as per Census 2001).

Subjects

All clinically suspected cases presented with symptoms such as prolonged fever, chronic cough and dyspnoea, chronic diarrhea, progressive weight loss, disseminated tuberculosis, oral thrush, herpes zoster and unexplained lymphadenopathy. All patients attending the in-patient and out-patient departments during this study period and belonging to Pokhara sub metropolitan city were included in the study. A total of 404 clinically suspected cases of HIV/AIDS were screened. Informed consent was taken and pre-test and post-test counseling was routinely done for all the by trained experts.

HIV testing and confirmation

HIV infection was confirmed when at least two of the following tests were positive; HIV 1 and 2 (Tri-Dot ELISA, J. Mitra & Co., Ltd., New Delhi, India), HIV-Spot (Eli scan, Ranbaxy, New Delhi), or HIV 1 and 2 Western blot (Gene Lab Diagnostics, Singapore) as recommended by WHO strategy – II of 1993.

Subject bio-data/Post test counseling

A total of 74 patients were found to be HIV positive. Information on age, sex, and educational status, mode of acquisition/transmission and clinical profiles of the HIV positive patients were obtained using a questionnaire. Based on the National Center for AIDS and STD Control (NCASC) guidelines, all the HIV positive cases were counseled and educated regarding different modes of transmission as this is helpful in controlling the spread infection.

Statistic analysis

The EPI-INFO soft ware package programme was used for the statistical analysis.

RESULTS

Table 1 shows that out of 404 suspected cases, 74 (18.3%) tested positive for HIV, with majority (74.32%) in the age group 20-39 years. Fifty nine (79.7%) of the HIV positive patients were males and 15

(20.3%) were females. The odds ratio calculated for HIV positivity in relation to sex was 3.16 (with CI 1.66 - 6.08) and p < 0.001 showing a strong association between HIV positivity and sex, with male preponderance.

Table 1 Distribution of HIV Positivity according to age and sex

Age group	HIV positive			HIV negative			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 (79.73)**	**15 (20.27)**	**74(100) (18.32)**	**183**	**147**	**330 (81.68)**	**404(100) (100)**

x^2 = 19.52, p < 0.001, Odds Ratio=3.16, Confidence Interval (CI) = 1.66 - 6.08

In Table 2, out of 404, 219 (54.2%) cases were illiterate. The proportion of illi-terate among HIV cases was 28.6% and proportion of cases with primary level education was 55.4%. Association between literacy and HIV positivity was found to be significant (X^2 = 24.93, p < 0.001).

Table 2: 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 3, the proportion of sex workers or clients of sex workers in HIV positive cases was found to be 60.8% and the proportion of intravenous drug users (IVDUs) was 21.6%. The proportion of vertical transmission from infected mother to the baby was found to be 4.05%. Association between factors responsible for transmission and HIV positivity was significant (X^2 = 25.70, p < 0.001). Table 4 shows that the commonest presenting symptom in HIV positive cases was fever (48.6%), followed by weight loss (36.5%), cough and dyspnoea (36.5%), chronic and recurrent diarrhoea 18.2%, and 28.4% and 21.6% for pneumonia and pulmonary respectively. The proportion of patients presenting with tuberculous meningitis (TBM) and disseminated TB was 5.4%. Slim's disease was seen in (5.4%) cases. Out of 74 HIV positive cases, 4 (5.4%) cases died giving a mortality rate of 5.4%.

Table 3: Distribution of the factors influencing modes of transmission of HIV

Factors	HIV Test		Total (%)
	Positive	Negative	
Commercial 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	9(12.16)	84	93(23.03)
Mother to child	3(4.05)	8	11(2.72)
Total	**74(100)**	**330**	**404(100)**

x^2= 25.70, p= < 0.001

Table 5 shows the distribution of infectious agents in the different types of clinical specimens obtained from patients in

the study. A total of 45 microbial isolates were recovered from the patients.

Table 4: Clinical profile of HIV positive patients

Clinical symptoms	HIV Test		Total
	Positive (N=74) (%)	Negative (N=330)	(N=404) (%)
Fever	36(48.65)	189(57.27)	225(55.69)
Weight loss	27(36.49)	107(32.42)	134(33.17)
Cough & dyspnoea	27(36.49)	113(34.24)	140(34.65)
Pneumonia	21(28.38)	97(29.39)	118(29.21)
Pulmonary TB	16(21.62)	49(14.85)	65(16.09)
Skin & mesothelial infection	13(17.57)	27(8.18)	40(9.9)
Recurrent diarrhea	12(16.22)	101(30.61)	113(27.97)
PGL	05(6.76)	1(0.3)	06(1.49)
TBM & Disseminated TB	04(5.41)	1(0.3)	05(1.24)
Extra-pulmonary Tubercular lymph node	07(9.46)	03(0.91)	
Depression	03(4.05)	17(5.15)	20(4.95)
Lymphoma	02(2.7)		
Slims disease	04(5.41)	1(0.3)	05(1.24)
Death	04(5.41)	1(0.3)	05(1.24)

[NB: PGL=persistent generalised lymphadenopathy, TB =tuberculosis, TBM= tubercular meningitis]

Mycobacterium tuberculosis constitute the majority with 60%, followed by *Cryptosporidium spp* 13.3%, *Candida albicans* 11.1%, *Cryptococcus neoformans* 6.7% and 2.2% each of *Isospora belli*, *Pneumocystis carinii*, *Strongloides stercoralis* and *Cyclospora spp.*

Table 5: Pathogens isolated in HIV infected patients (n = 45)

Organism	Specimen	No of patients (%)
Mycobacterium tuberculosis	Sputum	16 (35.5)
	Lymph node	7 (15.5)
	CSF	4 (8.8)
Cryptosporidium spp	Stool	6 (13.3)
Candida albicans	Oesophageal brush	5 (11.1)
Cryptococcus neoformans	CSF	3 (6.7)
Isospora belli	Stool	1 (2.2)
Pneumocystis carinii	Broncho-alveolar lavage (BAL)	1 (2.2)
Strongloidis stercoralis	Stool	1 (2.2)
Cyclospora spp	Stool	1 (2.2)
		45

DISCUSSION

In this study (hospital based cross-sectional study), 18.3% of a total of 404 patients screened for HIV were confirmed positive, with majority in the age group 20-39 years and with male preponderance (79.7%). These findings are consistent with otherstudies in Nepal (11) and elsewhere. The age group 20-39 years is an established high risk group for HIV infection world wide because this is the most sexually active group in any population.

In the study, literacy was significant -ly associated with HIV positivity ($x^2 = 24.93$, $p < 0.001$), with over 50% of those positive being literate above primary school education. This is similar to the finding of Sharma *et al* (12). The more literate a person is, the more sexual adventure he is likely to undertake, with a tendency to keeping multiple sexual partners, which is an identified high risk sexual behaviour.

The main mode of transmission in this study is predominantly heterosexual contact (60.8%) as attested to by a high proportion of sex workers and clients of sex workers testing positive. This agrees with reports of the study by Gurubacharya *et al* (13). One hundred and twenty nine (32.9%) of the 404 patients screened were intravenous drug users (IVDUs), out of which 16 (3.9%) were HIV positive. Published data (14) have indicated that intravenous drug abuse is a problem in many parts of Nepal. About 22% of the HIV positive patients in this study were IVDUs. This definitely calls for urgent health education campaign to these vulnerable youths on the danger of using unsterilized needles or sharing of needles when injecting drugs.

About 4% of cases seen were children who acquired the infection through vertical transmission. HIV infection in children born to symptomatic sero-positive mothers is yet another deplorable situation and remains the submerged stem of iceberg in the vast population of Nepal. This figure tallies with other studies done in other Asian countries (15).

The non-specific symptoms such as fever, weight loss, cough and dyspnoea seen in our patients were not different from those seen in other studies conducted in neighboring countries like India (16). HIV and TB synergy has a devastating impact in the developing world where 95% of the people live with dual menace of tuberculosis and HIV infection (17). The HIV surveillance in patients with tuberculosis in Nepal during 2001 and 2002 reveals a 2.4% prevalence of HIV in TB patients. HIV prevalence in TB patients continues to rise and has increased by 4-fold in the last 6 years. Moreover, 84 % of cases are in men aged above 25 years and in women all cases occurred in the under 25-year age group (18). In this study, pulmonary tuberculosis was found in 16 (21.6%) of HIV positive cases while *Mycobacterium tuberculosis* was isolated from lymph node and CSF as extra-pulmonary tuberculosis in 24.44%. These finding are comparable to similar studies conducted in Thailand (19) as well as in many other developing countries as reported by Raviglione *et al* (20).

Despite better understanding of the pathogenesis and clinical significance of weight loss in Slim's disease, not much has been done to improve the nutritional status of these patients during early stage of the disease. This is attributed to variety of constraints namely parasitic diarrhoea, depression, anorexia (drug or disease induced) and inescapable poverty (21). In the present study, we found 4 (5.4%) HIV positive cases with Slim's disease. This is the same picture in Zaire and Uganda where for the first time in early 1980's, Slim's disease, characterized by profound weight loss and chronic parasitic diarrhea, was recognized and where it was difficult to improve the nutritional status in the early stage for purely economic reasons (22).

The opportunistic pathogens and the infections they caused in our patients in this study have been described for most patients with HIV infection elsewhere in the world, and these infections are more pronounced at the terminal stage of the disease.

CONCLUSION

In this study, we found HIV positivity to be high in the 20-39 year age group, the group that is made up of the most economically productive unit of any society. We also found main mode of transmission to be heterosexual. Therefore, health education emphasizing practice of safe sex, avoidance of multiple sexual

partners, premarital and extramarital sex would go a long way in preventing the spread of HIV infection in the community. This can be achieved through mass media, use of video films, charts and posters.

To prevent mother to child transmission, it is necessary to educate mothers and adolescent females regarding benefits of antenatal care and making HIV screening mandatory in antenatal clinics, so that sero-positive mothers can have a choice of keeping or terminating the pregnancy.

The present study documents that tuberculosis, cryptosporidiosis and candidiasis are the most predominant opportunistic infections in 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.

Most of the studies on HIV carried out in Nepal are mainly hospital based due to limited resources. These do not give accurate information of the incidence and distribution of opportunistic infections by geographical or regional location. It is therefore necessary to conduct community-based studies, especially in inaccessible rural areas of Nepal where the situation is still not clear. It is also necessary to organize quarterly or half-yearly health campaign in the remote rural areas and encourage voluntary screening.

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