Abstract

Objective: Pneumocystis carinii pneumonia (PCP) is believed to be rare in the developing world and no large prospective Indian series have been reported to date. The present study was conducted to study the clinical profile and outcome of PCP in patients with HIV infection.

Methods: All HIV positive patients with PCP admitted over 4 years (2000-2003) to a tertiary referral centre in Mumbai were prospectively studied.

Results: There were 38 patients with proven PCP from 300 HIV admissions. The patients with PCP were predominantly male (M : F = 5.4 : 1), with a mean age of 40.1 years. The median CD4 count of the PCP group was 96 cells/µL. Bronchoscopy was needed to make a definitive diagnosis in 17 of the 38 patients. PCP co-existed with tuberculosis in 4 of the 38 patients. The mortality of the group was high at 15.8% with all patients needing ventilatory support dying.

Conclusions: PCP is not an uncommon infection in Indians with advanced HIV. Lack of recognition has probably been responsible for the absence of any large series from this country. In our series of hospitalised HIV positive patients, PCP was the second commonest pulmonary disease after tuberculosis accounting for 32% of pulmonary admissions and 13% of all HIV positive admissions.

INTRODUCTION

Tuberculosis (TB) and bacterial pneumonia dominate most HIV series from the developing world. In the first decade of the epidemic, Pneumocystis carinii pneumonia (PCP) was rarely reported from the developing world and authors concluded that PCP was uncommon in the developing world.1 Recent reports, however have noted a significantly higher prevalence of PCP among HIV-infected patients in Sub-Saharan Africa.2-3 Fisk et al in their comprehensive recent review of PCP in the developing world failed to find a single PCP series from India.4 Our study prospectively looked at all HIV positive patients hospitalised at a tertiary referral hospital with an active pulmonary service. From the 300 admissions over a 4 year period (2000-2003), we analysed the profile of the 38 patients with microbiologically confirmed PCP. This is the only large prospective PCP series from the Indian subcontinent and confirms that PCP is not uncommon here but has probably been under-recognized to date.

METHODS

All HIV positive admissions at our private hospital which is a tertiary referral centre had their clinical data prospectively collected over a 4 year period from 2000-2003. All patients proven to have PCP were included for separate analysis. From each patients’ records we obtained the following data: (1) age, sex, symptoms, signs, chest radiograph, high resolution computed tomogram (HRCT) of the chest features, arterial blood gas, lactate dehydrogenase (LDH) and CD4 count. (2) Methods needed to make a diagnosis of PCP; spontaneously expectorated sputum, induced sputum, bronchoalveolar lavage (BAL) fluid or transbronchial lung biopsy. (3) Details of treatment received by each patient. (4) Mortality in hospital.

All PCP diagnosis was performed by a single cytologist using an indirect immunofluorescence staining technique on sputum or BAL. The primary antibody was a mouse monoclonal anti-pneumocystic carinii from DAKOPATTS with a fluorescein isothiocyanate conjugated secondary rabbit anti-mouse antibody. Direct sputum smears and cytospin smears of BAL fluid were made, air dried, fixed in methanol-$H_2O_2$ and stained in a humidified chamber at room temperature. The smears were mounted in glycerine and viewed under a Zeiss fluorescent microscope. Apple
bronchoscopy from BAL fluid in 15 patients and from the other 17 patients. Thus the diagnosis was made at more invasive tests were needed to establish the diagnosis. gavie a microbiological diagnosis in 21 of the 38 patients, the TB-HIV patients. Whilst sputum (direct or induced) cells/µL in contrast to a median CD4 of 137 cells/µL in the patients who died in our series.

**RESULTS**

Thirty eight patients with PCP were obtained from the 300 HIV positive patients hospitalised over this 4 year period (2000-2003). PCP accounted for 13% of all HIV hospitalisations. If the HIV positive patients with pulmonary manifestations were analysed as a separate group (120 patients), PCP accounted for 32% of all pulmonary admissions and was second only to pulmonary TB which accounted for 40% of all pulmonary admissions. PCP was more frequent than bacterial pneumonia which was the 3rd most common pulmonary cause of admission.

The mean age of the PCP patients was 40.1 years (18-62 years) with a male to female sex ratio of 5:4:1 (32 males and 6 females). Cough was the commonest symptom (27/38), followed by dyspnoea (22/38) and fever (20/38). Only 1 patient was asymptomatic when the diagnosis of PCP was established.

The commonest respiratory sign was a respiratory rate > 26/min which was found in 25/38 patients with PCP. The respiratory rate was > 30/min in 15/38 patients. Fine crackles were found in 19/38 and ronchi in 6/38 patients. 9/38 patients were normal on examination.

The chest radiograph was reported as compatible with PCP with bilateral interstitial shadows in 29 patients. Chest radiographs were normal in 8 patients (21%) and atypical radiographic appearances (a solitary pulmonary nodule) were present in only 1 patient. HRCT chest scans were done in 18 of the 38 patients. Ground glass and nodules were present in HRCT chest scans of 17 of these 18 patients and were reported to be “highly suggestive of PCP”.

Nineteen of the 38 patients had a PaO2 < 70 mm Hg. LDH was checked in only 13 of the 38 patients and was found to be elevated in 12. A rising LDH level was found to be an important prognostic marker in all the 6 patients who died in our series.

The median CD4 count of the 38 PCP patients was 96 cells/µL in contrast to a median CD4 of 137 cells/µL in the TB-HIV patients. Whilst sputum (direct or induced) gave a microbiological diagnosis in 21 of the 38 patients, more invasive tests were needed to establish the diagnosis in the other 17 patients. Thus the diagnosis was made at bronchoscopy from BAL fluid in 15 patients and from transbronchial biopsy alone in 2 patients where sputum and BAL failed to identify PCP. Four patients (10.5%) had Mycobacterium tuberculosis isolated with their PCP in sputum or BAL samples.

All patients were initially treated with trimethoprim-sulfamethoxazole (TMP-SMX). Six patients however needed to be switched to a clindamycin-primaque combination because TMP-SMX proved ineffective (2 patients) or toxic (severe rash in 2, nephrotoxicity in 2). Steroids were used along with initial antibiotics in 19 PCP patients whose PaO2 was less than 70 mm Hg. Six patients required mechanical ventilation for worsening respiratory failure, all of whom died.

**DISCUSSION**

In the first decade of the HIV epidemic, PCP was considered an uncommon pathogen in the developing world. In studies from Zambia, Tanzania and Rwanda, PCP accounted for 3-9% of all hospitalised HIV patients with pneumonia. In studies from Asia, PCP accounted for a greater percentage of cases of pneumonia among African adult HIV infected patients than noted in earlier reports. More recent studies (1990-1993) from South Africa and Zimbabwe using more sophisticated diagnostic techniques like BAL and monoclonal antibodies revealed rates of PCP of 43% and 33% respectively.

Studies from Asia have been even less frequent. Fisk et al in their comprehensive review of PCP in the developing world found only a few Asian studies from Thailand, South Korea, Taiwan and The Philippines but none from India. We conducted a more detailed search focusing on PCP in Indian journals and found that Indian data on PCP was restricted to a few isolated case reports or small autopsy series but no large prospective series existed. The relevant Indian data is summarized here. The first case report on PCP in India was from Udwadia et al in a single case in 1987. This patient had advanced immunosuppression and died despite TMP-SMX and ventilatory support. In the 17 years since this first description of PCP, this disease has been considered rare in India as is evident from the scanty data available. There are a number of small PCP series of 2-5 cases written up mainly as case reports in Indian medical journals. Some series reported larger numbers but included patients where PCP was suspected on clinical and radiological grounds but not proven microbiologically.

There are some autopsy series and here mention must be made of work by Lanjewar from a large public hospital in Mumbai. He found evidence of PCP in only 7 of 143 (5%) lung autopsies. In his series, as in most autopsy series from this country, TB dominated, accounting for 60% of all cases. In the only other autopsy series reported
from our country, Deshmukh from Pune reported 5 cases of PCP out of 34 AIDS autopsies\textsuperscript{20}, whilst Santosh reported only 2 cases of PCP from 47 AIDS autopsies.\textsuperscript{21} Kumarasamy in his large cohort of 594 HIV patients from a tertiary referral centre in southern India reported 36 patients (6.1\%) with PCP.\textsuperscript{22} However details of these PCP patients as a group have not been discussed.

There have been various postulated reasons for the lack of PCP reports from India and the developing world including the absence of PCP from the environment, differences in host susceptibility to the organism and death at an earlier stage from more pathogenic organisms like \textit{Mycobacterium tuberculosis}.$^{23}$ In our opinion it is simply delayed recognition and lack of diagnostic facilities that are responsible for this under-reporting.\textsuperscript{24} As many as 45\% of our patients would not have been diagnosed if sputum alone had been tested. The bronchoscopic techniques required to make a firm diagnosis of PCP are not available in the majority of Indian hospitals. The availability of expensive immunofluorescent staining techniques, an experienced cytologist and the presence of a CT scanner are other luxuries beyond the reach of the average Indian hospital and these are the likely reasons for under-reporting of PCP from the Indian subcontinent.

We found a high prevalence of PCP in our series, accounting for 32\% of pulmonary admissions and 13\% of all hospitalized HIV positive admissions. The other interesting features of the PCP patients in our series are the co-existence of TB and PCP noted in 4 (10.5\%) of the patients. Other studies from the developing world have reported PCP and TB co-infection in 13-66\% of their patients.\textsuperscript{4} The mortality of our patients was also higher than in Western series with 15.8\% of PCP patients dying. This trend towards higher mortality has been noted in other series from the developing world and may be linked to lack of recognition leading to late diagnosis and treatment.

In conclusion, HIV-AIDS is gaining a firm foothold in India. With at least 4 million Indians already infected, India houses the world's second largest HIV positive population. Despite this there is almost no Indian data available on PCP, one of the commonest AIDS defining infections globally, from a country with a population of 1 billion. This study attempts to redress this imbalance and is the only large PCP series from India. It is almost certainly lack of awareness coupled with lack of access to special diagnostic tools that is responsible for the absence of data on PCP from the Indian subcontinent.

**References**


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**Book Review**

**Practical Approach to Respiratory Diseases with CD ROM**

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**Announcement**

Nominations are invited from members of API for the post of Editor - *Journal of the Association of Physicians of India*.

The nominations should be proposed and seconded by two members along with seven copies of the Biodata and should reach the Hon. General Secretary of API, Dr. **Sandhya Kamath**, by 15th July 2005. Unit No. 6 and 7, Turf Estate, Opp. Shakti Mill Compound, Off. Dr. E Moses Road Near Mahalaxmi Station West, Mumbai 400 011. Tel. 022-5666 3224; Fax : 2492 0263