# *PNEUMOCYSTIS CARINII* (*JIROVECII*) PNEUMONIA (PCP): THE MOST COMMON OPPORTUNISTIC INFECTION OBSERVED IN HIV/AIDS CASES AT THE UNIVERSITY MALAYA MEDICAL CENTRE, KUALA LUMPUR, MALAYSIA

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**Abstract.** This retrospective study was conducted among 59 HIV/AIDS patients with opportunistic infections admitted to the University Malaya Medical Centre between 2000 and 2009. Fifty-five point nine percent of cases were Chinese, 25.4% were Malays, 11.9% were Indians and 6.8% were of unknown ethnic origin. The male:female ratio was 2.9:1 (44 males and 15 females). The highest prevalence (38.9%) occurred in the 30-39 year old age group. Men comprised 47.7% and women 53.3%; the majority of both were married. The majority of cases were Malaysians (89.8%) and the rest (10.2%) were immigrants. Most of the patients (18.6%) were non-laborers, followed by laborers (11.9%), the unemployed (5.1%) and housewives (3.4%). The most common risk factor was unprotected sexual activity (20.3%). The two most common HIV/AIDS related opportunistic infections were *Pneumocystis carinii (jirovecii)* pneumonia (PCP) (62.7%) and toxoplasmosis (28.8%). Seventy-two point nine percent of patients had a CD4 count <200 cells/ l and 5.1% had a CD4 count >500 cells/ l. Eleven point nine percent of cases died during study period. A low CD4 count had a greater association with opportunistic infections. Most of the patients presented with fever (44.1%), cough (42.4%) and shortness of breath (28.8%). Detection of the etiologic pathogens aids clinicians in choosing appropriate management strategies.

**Keywords:** *Pneumocystis jirovecii*, HIV/AIDS patients, opportunistic infection, Malaysia

## INTRODUCTION

Acquired immune deficiency syndrome (AIDS) is a disease of the human immune system caused by the human immunodeficiency virus (HIV). AIDS is a pandemic (Anthony *et al*, 1998). In 2007, UNAIDS estimated 33 million people worldwide had AIDS. AIDS has killed approximately 2 million people, including 330,000 children; 76% of the deaths occurred in sub-Saharan Africa (UNAIDS, WHO, 2007).

The clinical signs and symptoms of AIDS occur as a result of conditions that do not normally develop in persons with normal immune systems. Opportunistic infections are common in people with AIDS (Anthony *et al*, 1998).

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In Malaysia, the first reported case of AIDS was in 1986 (Ismail *et al*, 1995). There now have been more than 86,000 reported cases of HIV infection in Malaysia (MOH, 2010). The majority of new HIV infections are found among adults aged 20 to 29 years (32.5% of cases in 2003 and 24.9% of cases in 2008) and among those aged 30 to 39 years (41.8% of cases in 2003 and 42.2% of cases in 2008), which is the age range in which citizens are the most productive (MOH, 2010). A high rate of HIV transmission has been found among intravenous drug users (IVDU) (70% of cases in 2003 and 53.2% of cases in 2008) (MOH, 2010). The number of infections transmitted through heterosexual intercourse has increased from 19% of cases in 2003 to 26.8% of cases in 2008 (MOH, 2010). The number of HIV positive women has been increasing as well. In 2000, 9.5% of new HIV infections were among women, in 2004 this increased to 10.8% of cases and in 2008 it was 19.1% of cases (MOH, 2010). Ninety-one percent of people living with HIV in Malaysia are men. In 2008, the number of women living with HIV in Malaysia had increased to 19% (MOH, 2010). Fifteen Malaysians are diagnosed every day with HIV infection (MOH, 2010). Thirty-four percent of newly reported cases in Malaysia are in their twenties (MOH, 2010). In 20 years, the number of new HIV cases expected in Malaysia will have increased by 883% (MOH, 2010). AIDS has caused the deaths of more than 10,000 Malaysians (MOH, 2010).

*Pneumocystis jirovecii* (formerly known as *Pneumocystis carinii*) is an opportunistic fungal organism that causes *Pneumocystis jirovecii* Pneumonia (PCP) in humans. *Pneumocystis* causes disease in immunocompromised individuals, particularly those infected with HIV. PCP is the most common opportunistic infection in patients with AIDS (Kelly and Shellito, 2010). Its incidence has decreased greatly with the advent of highly active antiretroviral therapy (HAART). An increase in non-HIV immunocompromised individuals (Kelly and Shellito, 2010), noncompliance with antiretroviral treatment and emergence of drug-resistant strains of HIV in developing countries had made *Pneumocystis* a pathogen of continued interest and a public health threat. A great deal of research has gone into the treatment of waning immunity and the prevention and treatment of PCP (Kelly and Shellito, 2010).

Liam and Wang (1992) studied nine patients with systemic lupus erythematosus (SLE) treated for PCP between 1987 and 1988 at the University Hospital Kuala Lumpur, Malaysia. Ismail *et al* (1995) found the most common AIDS-defining illness was PCP. Yoong and Cheong (1997) carried out a cross sectional study to determine the clinical profile, hematological and biochemical changes, seroprevalence of common opportunistic pathogens and AIDS-defining events among 49 Malaysian male drug addicts with HIV infection. Pulmonary infection was the most common complication seen (61%); four had PCP. Cheong *et al* (1997) conducted a study of 334 patients infected with HIV at the Hospital Kuala Lumpur. The two commonest opportunistic infections were tuberculosis (36%) and PCP (23%). Wood *et al* (1998) carried out a retrospective study of 144 adults with HIV infection and found tuberculosis (40%) and bacterial pneumonia (33%) comprised the majority of lower respiratory tract infections (LRTI) among intravenous drug users, while PCP (40%) was the commonest LRTI amongst the other-risk group. Nissapatorn *et al* (2003) reviewed 419 HIV/AIDS patients at Hospital Kuala Lumpur. The four main AIDS-defining illnesses were tuberculosis

Table 1
Prevalence of opportunistic infections among HIV/AIDS patients by age, race and sex at the University Malaya Medical Centre (UMMC) from 2000 - 2009.

| Race | Malay | | Chinese | | Indian | | Others | | Total (%) |
|---|---|---|---|---|---|---|---|---|---|
| Age (Years) | Male | Female | Male | Female | Male | Female | Male | Female | |
| 20-29 | 3 | 1 | 4 | 1 | | 1 | | 1 | 11 (18.6) |
| 30-39 | 4 | 1 | 10 | 3 | | 4 | 1 | | 23 (39.0) |
| 40-49 | 5 | | 10 | 1 | 2 | | 1 | 1 | 20 (33.9) |
| 50-59 | | | 2 | | | | | | 2 (3.4) |
| 60-69 | | 1 | 2 | | | | | | 3 (5.1) |
| Total (%) | 12 (20.3) | 3 (5.1) | 28 (47.5) | 5 (8.5) | 2 (3.4) | 5 (8.5) | 2 (3.4) | 2 (3.4) | 59 |

(48%), PCP (13%), toxoplasmic encephalitis (11%) and cryptococcal meningitis (7%). Fifty-three percent of these patients had a CD4 cell count <200 cells/ l. Asmal *et al* (2009) reviewed 107 AIDS cases and found PCP was the most common opportunistic infection in patients with a CD4 count ≤200 cells/ l. The incidence of PCP has declined as a result of prophylaxis and treatment with HAART. Asmal *et al* (2009) also reported PCP can occur in patients with a CD4 count >200 cells/ l. All these studies reported PCP was the most common opportunistic pathogen among HIV/AIDS patients in Malaysia.

The aim of this retrospective study is to determine the prevalence of opportunistic infections among HIV/AIDS infected patients at the University of Malaya Medical Centre (UMMC), Kuala Lumpur over the past 10 years (2000-2009).

## MATERIALS AND METHODS

A total of 59 cases of HIV/AIDS with opportunistic infections from January 2000 to December 2009 were reviewed.

The data were entered and analyzed using SPSS, version 17 (SPSS, Chicago, IL). Data with quantitative variables were expressed as medians ± SD and ranges, whereas qualitative variables were expressed as frequencies and percentages.

## RESULTS

The age range of patients was 20 to 69 years with a median of 39.0 (+ 9.31 years). The male:female ratio was 2.9:1.

Table 1 shows that 39% of cases (23/59) occurred in the 30-39 year old age group. The majority (55.9%, 33/59) were Chinese, followed by Malays (25.4%, 15/59), Indians, (11.9%, 7/59) and others (6.8%, 4/59). The majority of cases (74.6%, 44/59) occurred among males. The most common cases were among Chinese males, (47.5%, 28/59). Forty-seven point seven percent of males (21/44) and 53.3% of females (8/15) were married. Fifty-three cases (89.8%) were Malaysians and 6 cases (10.2%) were immigrants. Eleven point nine percent of cases (7) were laborers, 18.6% (11) were non-laborers, 3.4% (2) were housewives and 5.1% (3) were unemployed. Sixty-one percent (36) had no specified occupation.

The most common risk factors (Fig 1) were unprotected sexual activity (20.3%, 12/59), chronic smoking and alcohol consumption (18.6%, 11/59), having multiple

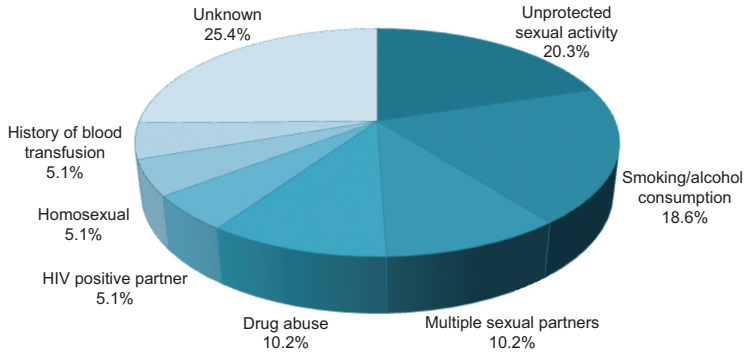


Fig 1–Risk factors among HIV/AIDS patients with opportunistic infections seen at UMMC during 2000-2009.

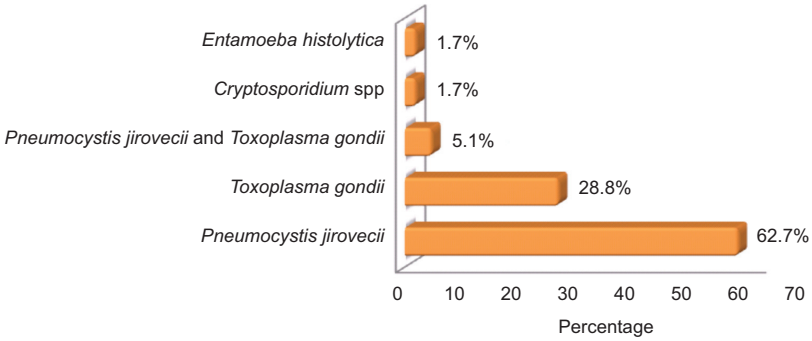


Fig 2–Type of opportunistic organisms among HIV/AIDS patients seen at UMMC during 2000-2009.

sexual partners (10.2%, 6/59) and drug abuse (10.2%, 6/59). Minor risk factors in this study were having an HIV positive partner, being homosexual, and having a history of blood transfusion (5.1%, 3/59 each). Unknown risk factor constituted 25.4% of cases (15/59).

Most of the patients (62.7%) suffered from PCP (Fig 2). Toxoplasmosis was the second most common infection (28.8%) among HIV patients. Three cases (5.1%) had mixed PCP and *Toxoplasma gondii* infections, 1 case (1.7%) had cryptosporidiosis and 1 case (1.7%) had a persistent amebic liver abscess.

Fig 3 shows most opportunistic infections (72.9%) occurred among HIV patients with a CD4 count <200 cells/ l. Only 5.1% of cases with an opportunistic infection had a CD4 count >500 cells/ l.

Most patients presented with fever (44.1%), cough (42.4%) or shortness of breath (28.8%). Eighty-eight point one percent of patients recovered, while 11.9% died during hospitalization.

## DISCUSSION

Numerous opportunistic infections can occur in HIV/AIDS infected patients, due to the suppressed immune system. This highlights the need for early detection and treatment of opportunistic infections among HIV/AIDS infected patients to reduce morbidity and mortality.

In this study *Pneumocystis jirovecii* (62.7%) was the most common opportunistic infection followed by *Toxoplasma gondii* (28.8%). Studies from other parts of the world have reported similar findings (Mahomed, 1999; Radhi *et al,* 2008; Huang and Crothers, 2009; Fei *et al,* 2009; Enomoto *et al,* 2010; Gray and Zar, 2010; Kelly and Shellito, 2010; Mahdavi *et al,* 2010; Morrow *et al,* 2010). In our study, similar to previous reports, *Cryptosporidium spp* (Kucerova *et al,* 2010) and *E.*

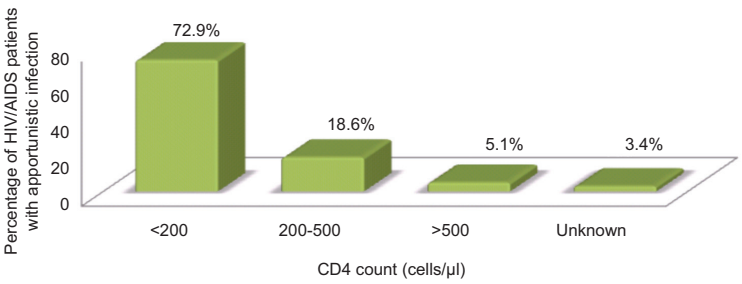


Fig 3–CD4 count upon presentation among HIV/AIDS patients with opportunistic infections seen at UMMC during 2000-2009.

*histolytica* were detected in only a few patients (Daryani *et al*, 2009).

The most common opportunistic infection among HIV/AIDS patients at UMMC was PCP, similar to the findings of other studies from other localitions in Malaysia (Wood *et al*, 1998; Asmal *et al*, 2009).

The majority of patients with opportunistic infections in our study had CD4 count < 200 cells/ l, the majority of opportunistic infections being PCP, similar to other studies (Feldman, 2005; Asmal *et al*, 2009).

*Pneumocystis* is an unicellular fungus found in the respiratory tracts of mammals and humans. It was previously considered a sporozoan parasite until molecular analysis showed its closer relationship to fungi than to protozoa (Bennett and Gilroy, 2010). *P. jirovecii* is one of several organisms known to cause life-threatening opportunistic infections among patients with advanced HIV infection worldwide. Over 100,000 cases of PCP were reported during the first decade of the HIV epidemic in the United States among people with no other cause for immunosuppression (Bennett and Gilroy, 2010). *Pneumocystis* organisms are commonly found in the lungs of healthy individuals (Bennett and Gilroy, 2010). Most children are believed to have been exposed to the organism by age 3 or 4 years, and its occurrence is worldwide (Bennett and Gilroy, 2010).

Opportunistic infections are late complications of HIV infection; for the most part occurring in patients with a CD4 cell count <200 cells/ l. Infections with PCP probably represent reactivation of latent infection or failure of host defense mechanisms to suppress a ubiquitous microorganism (Anthony *et al*, 1998).

Disease occurs when both cellular immunity and humoral immunity are defective. Once inhaled, the trophic form of *Pneumocystis* attaches to the alveoli. Multiple host immune defects allow for uncontrolled replication of *Pneumocystis* organisms and development of illness. Activated alveolar macrophages without CD4 cells are unable to eradicate *Pneumocystis* organisms (Bennett and Gilroy, 2010).

The typical clinical presentation of pneumocystosis is severe respiratory symptoms out of proportion to the physical and radiographic findings. Symptoms may include dyspnea, tachypnea, cough, intercostal retractions, nasal flaring and cyanosis, yet rales or signs of consolidation are not usually found on physical examination and no obvious pulmonary infiltrates can be detected on chest radiography. This phenomenon is probably due to an alveolar capillary block caused by the attachment of the trophozoites of *Pneumocystis* to the alveolar walls. Interstitial fibrosis, emphysema, pulmonary

calcification and cor pulmonale have been reported as complications of PCP. Diagnosis of PCP consists of examination of sputum or bronchoalveolar lavage using Giemsa stain (eight sporozoites surrounded by an unstained halo) or using Gomori's methenamine-silver stain (cup shaped structures) (Tsieh, 1988). At UMMC, immunofluorescence is used for demonstrating cysts, a serological test (ELISA) to diagnose toxoplasmosis, Ziehl-Neelsen staining and a crypto-strip test are used to diagnose *Cryptosporidium* spp and a serological test (IHA) is used to diagnose *E. histolytica*.

Before the advent of effective diagnosis, treatment and routine prophylaxis in Western countries, PCP was a common immediate cause of death among HIV patients. In developing countries, it is still one of the first indications of AIDS in undiagnosed individuals, although it does not generally occur unless the CD4 count is <200 cells/ l (Feldman, 2005).

Although PCP is classified as fungal pneumonia, it does not respond to antifungal treatment, but is treated with antibiotics. Treatment of PCP depends on the degree of illness at diagnosis, and is based on the alveolar-arterial gradient. It is recommended to use trimethoprim-sulfamethoxazole (bactrim) as first line treatment (Bennett and Gilroy, 2010). This combination has proved to be as effective as intravenous pentamidine and more effective than other alternative treatment regimens. It can be administered intravenously in patients presenting with serious illness or in those with gastrointestinal side effects (Bennett and Gilroy, 2010). The recommended duration of treatment for PCP is 21 days in patients with HIV infection and 14 days for all other patients (Bennett and Gilroy, 2010). Patients with moderate to severe PCP should receive corticosteroid therapy in addition to antibiotics. The most commonly used corticosteroids are oral prednisone or intravenous methylprednisolone.

Antiretroviral chemotherapy were commonly used at UMMC to control HIV infection includes Combivir, efavirenz, lamivudine and stavudine. Bactrim is commonly added to treat PCP; pyremethamine and sulphadiazine are used to treat toxoplasmosis.

Opportunistic infections among HIV/AIDS patients are still prevalent in Malaysia. Preventive and control measures, which include public health education, should be consistently implemented throughout the country. Prompt diagnosis and early treatment of HIV should help to prevent high morbidity and mortality.

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