RELATIONSHIP BETWEEN THE OCCURRENCES OF PENICILLIOSIS WITH CD4 LEVEL IN HIV INFECTED PATIENTS AND IMPACT ON CERTAIN HAEMATOLOGICAL PARAMETERS - ONE YEAR RETROSPECTIVE STUDY

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ABSTRACT

BACKGROUND

Since Manipur being a state with huge burden of HIV and AIDS, studies like these to evaluate certain uncommon opportunistic infections elsewhere which comes across in our day-to-day patient care need further evaluation for better management in times to come. Thus, this study was conducted with objective to assess the frequency of Penicilliosis cases in HIV patients in relation to the levels of CD4 count and impact on few selected haematological parameters in the referral hospital, JNIMS, Porompat, Imphal.

MATERIALS AND METHODS

A retrospective study was conducted by reviewing 8 medical records of confirmed cases of Penicilliosis from October, 2015 to September, 2016. All the cases were evaluated in accordance with the parameters namely Age, Sex, HCV co-infections, CD4 levels and levels of haemoglobins.

RESULTS

Among HIV patients in this study, Erythrocyte sedimentation rate (ESR) was between 50 to 100 mm/1st hour. Penicilliosis was very high among the age group of 40 to 60 years (63%). The prevalence of Penicilliosis was equal in both male and female patients. Co-infection with HCV did not affect the prevalence of Penicilliosis among HIV patients (25%). Incidence of Penicilliosis was commonest (37.5%) among those patients whose CD4 counts were below 50/cu.mm. The prevalence of Penicilliosis was highest (63%) among patients with HIV whose haemoglobin levels were between 5 to 10 g/dL.

CONCLUSIONS

Penicilliosis is very frequent in the age group of 40 to 60 years. There is apparently no gender preponderance and co-infection with HCV does not affect prevalence of Penicilliosis in HIV infected patients in this study. Prevalence of Penicilliosis among HIV patients whose CD4 count below 50/cu.mm was highest in the study; however, a vast majority of patients whose CD4 count above 50/cu.mm were noted to have penicilliosis. High ESR levels were noted in majority of HIV patients with Penicilliosis in the present study.

KEYWORDS

Penicilliosis, HIV, CD4 Count, HCV Co-Infection, Haemoglobin and ESR Level, JNIMS, Imphal, Manipur.

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BACKGROUND

Manipur is a small state in the north-eastern part of India with huge burden of people living with HIV.¹ A study like this on Penicilliosis is extremely important to analyse this life threatening opportunistic infection that is prevalent among the people living with HIV for better management in the diversity of the local population.

Penicilliosis is caused by a dimorphic fungus *Penicillium marneffei*, first discovered in 1959 by G. Segretain at the Pasteur Institute in Paris.² The first natural human infection was reported in 1973 from a patient with Hodgkin lymphoma

who lived in Southeast Asia³ and the first case in a patient with the human immunodeficiency virus (HIV) was reported in 1988.⁴ Since then several cases of Penicilliosis in patients of HIV had been diagnosed and it is particularly more common in Southeast Asia.⁵ In Thailand, penicilliosis has become the third most common illness that defines AIDS.⁶ Due to this rapid growth in the number of patients of Penicilliosis in HIV pandemic, it has become one of the commonest acquired immune deficiency syndrome (AIDS) defining illnesses among HIV positive patients in endemic areas.^{7,8,9}

Still very little is known about the natural reservoir and route of transmission of *P. marneffei*. Human and bamboo rats are the only known animal hosts of *P. marneffei*. Four species of bamboo rats, *Rhizomys sinensis*, *Rhizomys pruinosus*, *Rhizomys sumatrensis* and *Cannomys badius* are known to be enzootic reservoirs. The distribution of these bamboo rat species generally follows the distribution of endemicity of *P. marneffei*.^{10,11,12} In north-eastern part of India, bamboo forest is very common and so also bamboo rat, in Manipur we call it 'Shabi' which is a species of bamboo rat, *Cannomys badius*.

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MATERIALS AND METHODS

Data

A retrospective review of the Medical Records of the HIV positive patients admitted to the Department of Medicine, Jawaharlal Nehru Institute of Medical Sciences (JNIMS), Imphal were undertaken over a period of 12 months from October, 2015 to September, 2016. In this review, 8 patients were found to have Penicilliosis and details were entered in a systematic master chart after cross checking by many doctors separately. All the patients were on ART at the time of diagnosis of Penicilliosis. The parameters used in the present study include age, sex, CD4 count, HCV co-infection, haemoglobin and ESR (Erythrocyte sedimentation rate) levels.

Age

We have divided the age groups into four groups under this study as follows:

1. Age group below 20 years.
2. Age group between 20 to 40 years.
3. Age group between 40 to 60 years.
4. Age group above 60 years.

Sex

Prevalence of penicilliosis according to male and female gender variation was evaluated.

Co-infection with HCV

In this study, we have attempted to see for any variation in the incidences of Penicilliosis infection in HIV positive cases who are HCV co-infected and non-HCV co-infected.

CD4 Counts

Six groups were divided in an attempt to document the prevalence of Penicilliosis with mild changes in levels of CD4 counts, in HIV infected individuals in this study. The six groups are as follows:

1. CD4 count below 50 cells/cu.mm.
2. CD4 count between 50 to 100 cells/cu.mm.
3. CD4 count between 100 to 150 cells/cu.mm.
4. CD4 count between 150 to 200 cells/cu.mm.
5. CD4 count between 200 to 250 cells/cu.mm.
6. CD4 count above 250 cells/cu.mm.

Haemoglobin Levels

Changes in the level of haematological parameters i.e. Haemoglobin levels were also attempted to evaluate in accordance to the infection with Penicilliosis in HIV patients in this study. We have divided the Haemoglobin levels into four groups as follows:

1. Haemoglobin level below 5 g/dL.
2. Haemoglobin level between 5 to 10 g/dL.
3. Haemoglobin level between 10 to 15 g/dL.
4. Haemoglobin level above 15 g/dL.

Erythrocyte Sedimentation Rate (ESR)

The most neglected parameter worldwide in special connection to infection with Penicilliosis in HIV patients i.e. ESR, was taken up for evaluation in this study to document for any change in the background of Penicilliosis infection in HIV

patients. We have divided ESR levels into three groups as follows:

1. ESR level below 50 mm/1st hour.
2. ESR level between 50 to 100 mm/1st hour.
3. ESR level above 100 mm/1st hour.

Statistical Analysis

All statistical analyses were performed using Microsoft Office Excel.¹³ Mean, median and average were calculated for variables which are distributed normally. The data entered in the master chart of this study were interpreted using simple tools like percentage.

RESULTS

At the end of this study, 8 patients of Penicilliosis were documented among those HIV positive patients admitted to JNIMS Hospital over the study period of one year.

Among the age group, 20 to 40 years group had maximum number of Penicilliosis, about 63% of the total and was followed by 40 to 60 years group with 37% of Penicilliosis cases in the total number of Penicilliosis cases in HIV infected patients in this study [Figure 1].

Figure 1. Age Distributions of Penicilliosis in HIV Patients

In the present study, there was evidence of equal distribution of Penicilliosis cases in both male and female genders, each had 50% cases of Penicilliosis among the total HIV positive Penicilliosis infected patients [Figure 2] [Figure 2a] [Figure 2b].

Figure 2. Gender Distribution of Penicilliosis

Figure 2a. A Female Patient Admitted in Medicine Ward, JNIMS with Penicilliosis

Figure 2b. Microscopic Picture of Skin biopsy Showing many Yeast forms of Fungus both Intracytoplasmic and Extracytoplasmic, and Binary Fission Morphology consistent with Penicillium marneffei

Co-infection with HCV had contributed only 25% of Penicilliosis in patients with HIV infection in this study. A vast majority, that is 75% of the Penicilliosis cases were non-HCV co-infected HIV positive cases [Figure 3].

Figure 3. Number of Penicilliosis Cases in Relation to HCV Co-infection

Penicilliosis was most common in the HIV positive patients whose CD4 counts were below 50 cells/cu.mm accounting for 37.5% of the cases. It was closely followed by the group with CD4 count between 50 to 100 cells/cu.mm representing 25% cases of Penicilliosis in the study; 12.5% cases each in CD4 count groups between 100 to 150 cells/cu.mm, 200 to 250 cells/cu.mm and above 250 cells/cu.mm. Coincidentally, no patient was documented in the CD4 count between 150 to 200 cells/cu.mm [Figure 4].

Figure 4. Occurrence of Penicilliosis in Relation to CD4 Levels

Majority (63%) of the patients had Haemoglobin levels between 5 to 10 g/dL, it was followed by the group with Haemoglobin levels between 10 to 15 g/dL accounting for about 37% of the total number of Penicilliosis in HIV patients and there were no documented cases whose Haemoglobin levels were either below 5 g/dL or above 15 g/dL [Figure 5].

Figure 5. Haemoglobin Levels of Patients with Penicilliosis in HIV

Another haematological parameter evaluated in the study was the levels of Erythrocyte Sedimentation Rate (ESR). 50% of the Penicilliosis in HIV under this study had ESR between 50 to 100 mm/1st hour and 25% cases each in the group with ESR levels below 50 mm/1st hour and above 100 mm/1st hour [Figure 6].

Figure 6. Erythrocyte Sedimentation Rate in Penicilliosis with HIV

DISCUSSION

In the present study, 8 patients of Penicilliosis in HIV infected patients were documented. We had evaluated in different parameters as mentioned above in the materials and methods. Young adults of 20 to 40 years age group had maximum number of Penicilliosis in this study and was followed by 40 to 60 years age group. This finding is supported by studies done in Southeast Asia.¹⁴

In this study, male and female patients had equal predilections to Penicilliosis in HIV. This finding is in contradiction to the previously documented male preponderance in the studies done in Southeast Asian countries.^{14,15}

Hepatitis C co-infection in HIV patients does not seem to increase the predilection to Penicilliosis as evident from the present study.

In the present study, Penicilliosis was most common in the HIV positive patients whose CD4 counts were below 50 cells/cu.mm and was closely followed by the group with CD4 count between 50 to 100 cells/cu.mm. Similar finding has been documented in various studies conducted in different countries.^{10,14,16}

Haematological parameter changes were evaluated by measuring the Haemoglobin levels in these patients of HIV at the time of diagnosis of Penicilliosis. Majority of the patients of Penicilliosis with HIV in this study had Haemoglobin levels between 5 to 10 g/dL. Identical finding had been documented in previous studies done in Southeast Asian countries.^{14,17,18}

In this study, the levels of Erythrocyte Sedimentation Rate (ESR) of the penicilliosis in HIV patients had been on higher side between 50 to 100 mm/1st hour suggesting an increase in inflammatory process associated with infection with Penicilliosis.

CONCLUSION

Penicilliosis is still an important opportunistic infection in HIV patients of north-eastern part of India. It is particularly more common in young adults and is equally prevalent in both male and female patients in this study. Co-infection with HCV does not seem to increase the chance of acquiring Penicilliosis in HIV infected patients in this study. Low CD4 level has been shown to be associated with higher chance of acquiring Penicilliosis. Moderately, low haemoglobin levels were very common in Penicilliosis with HIV. Least studied parameter worldwide, ESR level in these groups of patients was on higher side. Further studies in larger perspectives are required for better understanding and better management with respect to local demographic variations.

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