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A clinical study of newly diagnosed HIV patients at VCTC, Wenlock hospital with correlation to CD4+ at presentation

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Abstract
Objectives: 1. To study the baseline values of CD4+ count in patients newly diagnosed to be infected with Human Immunodeficiency Virus(HIV) by the Voluntary Counselling And Testing Centre (VCTC) and hence determine how early during the natural course of the disease these patients are detected by VCTC.
2. To study the correlation between CD4+ cell counts and various opportunistic infections in HIV.
Methods: Study Site: Voluntary Counselling and Testing Centre (VCTC), Wenlock Hospital, Mangalore, Karnataka
Design: Cross Sectional Study
Subjects: Subjects under study were hundred consecutive newly diagnosed HIV patients in VCTC of all age groups and either gender, either asymptomatic or presenting with one or other opportunistic infections.
Results: Of the 100 patients studied between Sep 2007 and Mar 2009, 74% were males and 26% were females with male to female ratio of 2.8:1. The age at presentation varied from 14 yrs to 55 yrs with the majority between 35 - 40 yrs (28%). 99% of the study subjects acquired HIV through heterosexual contact. Of the 98 patients who were symptomatic, 78% had fever, 70% had cough, 66% had weight loss. Other symptoms included dyspnea (28%) and diarrhea (10%). Oropharyngeal candidiasis was the commonest opportunistic infection at presentation (76%) followed by tuberculosis (54%) of which meningeal tuberculosis was the commonest form (14%). Other tuberculous infections detected were pulmonary (12%), lymphadenitis (10%), disseminated (8%), pleural effusion (4%), miliary (2%), abdominal (2%) and endometrial (2%).Other opportunistic infections included pneumocystis pneumonia (10%), cryptosporidium (6%), herpes zoster (4%) and cryptococcal meningitis (4%). The minimum CD 4 count among the individuals studied was 10 cells/µl whereas the maximum was 499 cells/µl with a mean value of 180 cells/µl. Majority had a CD 4 count of ≤ 200 cells/µl (64%). 62 of the 76 patients with candidiasis had CD 4 count <200. All 14 patients diagnosed to have meningeal tuberculosis had a CD 4 count of < 200. The majority of pulmonary tuberculosis occurred between a CD 4 count of 200-400 cells/µl. All the other extrapulmonary forms of tuberculosis occurred most frequently at a CD 4 count of < 200 cells/µl. All cases of pneumococcal pneumonia, cryptococcal meningitis, majority of herpes and cryptosporidium infections occurred at a CD 4 count of <200 cells/µl.
Conclusion: Despite the efforts being put by the Government of India for early detection of HIV infection by establishing VCTCs in every state, we were unable to trace individuals at an earlier stage in the course of HIV infection. The patients being diagnosed with HIV infection presented with one or more of the opportunistic infections and frequently had a CD 4+ count < 200 cells/µl. This calls for increasing awareness about HIV in the general population so as to identify the disease at the earliest.

Keywords: CD4+ count, HIV, VCTC, Wenlock Hospital

Introduction

AIDS (Acquired Immunodeficiency Virus) is a severe disease syndrome that represents the late clinical stage of infection with HIV (Human Immunodeficiency Virus). The syndrome was first recognized in 1981, but probably existed at a low endemic level in Central Africa before epidemic HIV spread began to occur in several areas of the world during the 1970s [1]. Although HIV was introduced much later in Asia than the rest of the world, over 4 million people are now thought to be infected [2].

WHO estimates that with continued escalation of HIV transmission, nearly 9 million HIV-infected people will reside in South-East Asia by the turn of the century. National Aids Control Organization (NACO) estimates that by year 2025 the majority of new HIV infections in the world will occur in Asia and India will probably have the largest number of infected persons of any single country. Two new infections occur every minute in India [3, 4].

In an effort to curb the devastating impact on our society of HIV infection, termed the "greatest pandemic of modern times", NACO has introduced Voluntary Counseling and Testing Centres (VCTCs) in India, having a role in both HIV prevention and as an entry point to care [5].

Voluntary Counseling and Testing is the process by which an individual undergoes counseling enabling him or her to make an informed choice about being tested for HIV [6].

Potential benefits of Voluntary Counseling and Testing are

- Improved health status through good nutritional advice
- Earlier access to care and treatment
- Prevention of HIV related illness
- Emotional support
- Better ability to cope with HIV related anxiety

- Awareness of safer options for reproduction and infant feeding
- Motivation to initiate or maintain safer sexual practices
- Motivation for drug related behavior
- Safer blood donation [7]

This study was a sincere effort to study the baseline values of CD4+ count in patients newly diagnosed to be infected with Human Immunodeficiency Virus (HIV) by the Voluntary Counseling and Testing Centre and hence determine how early during the natural course of the disease these patients were detected by VCTC.

Aims and Objectives

The following were the aims and objectives of this study:

- To study the baseline values of CD4+ count in patients newly diagnosed to be infected with Human Immunodeficiency Virus (HIV) by the Voluntary Counselling and Testing Centre (VCTC) and hence determine how early during the natural course of the disease these patients were detected by VCTC.
- To study the correlation between CD4+ cell counts and various opportunistic infections in HIV.

Materials and Methods

Type of Study: CD4+ count done on blood sample collected from HIV infected patients in Govt. Wenlock Hospital.

Subjects under study: Subjects under study were hundred consecutive newly diagnosed HIV patients of all age groups and either gender.

Inclusion criteria: All newly diagnosed HIV patients in VCTC either asymptomatic or presenting with one or other opportunistic infections were included in the study.

Exclusion Criteria

- Patients with all other immune compromised states such as malignancies, organ transplant recipients, patients on corticosteroids or immunosuppressive therapy were excluded from the study.
- Patients on ART were excluded from the study.
- HIV seropositive individuals whose CD4+ T cell count could not be done were also excluded from the study.

Methodology

All HIV positive patients satisfying the inclusion and exclusion criteria were registered in the study group. These individuals were subsequently assessed thoroughly as per the protocol. This included a detailed clinical history and a complete physical examination followed by appropriate baseline and specific laboratory tests to identify the nature and extent of opportunistic process if any present. HIV infection was confirmed according to NACO and VCTC guidelines and assessment of the HIV related immune status was made by estimating the CD4+ cell counts.

Lab procedures

- HIV diagnosis
  1. Coomb's Test
  2. Tridot Test
  3. Capillar Test
- CD4+count done in Mysore Medical College.

Statistical Methods

Statistical package spss version 16.5 was used for the analysis.

Ethical Consideration

- Confidentiality of the data collected was maintained.
- All invasive procedures were done after taking consent.

Results

Sex Distribution: Of the 100 patients studied, 74% were males and 26% were females. The male to female ratio was 2.8:1

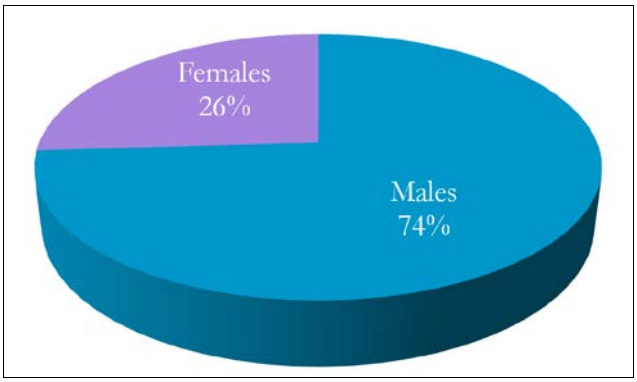

Fig 1: shows the sex distribution of individuals in this study

Age: The age of patients in this study ranged from 14 yrs to 55 yrs. The majority of the patients were in the age group between 35 - 40 yrs (28%).

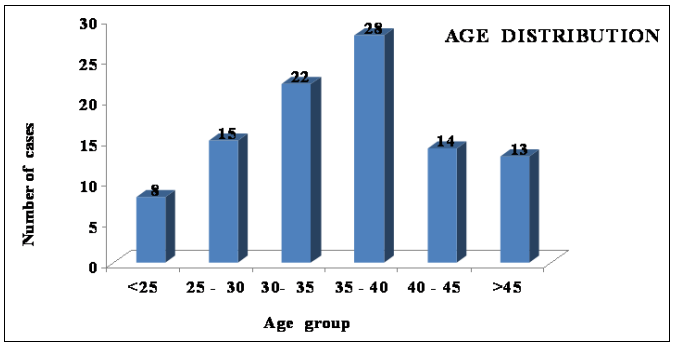

Fig 2: shows the age distribution of patients in this study

Mode of Transmission: Heterosexual contact (mainly polygamous) was the common risk factor in all. Significantly up to 99% subjects of the study group admitted to promiscuous contact clustered in and around Mangalore, while 1 patient acquired infection through vertical transmission.

Table 1: shows modes of transmission of HIV in this study

Mode of transmission	Frequency (%)
Sexual	99
Vertical	1

Symptoms at Presentation: Out of 100 patients, 2 patients were asymptomatic while 98 patients were symptomatic. The symptom profile in the study patients was as follows:

Table 2: shows symptom profile of the patients in this study

Symptoms	Frequency (%)
Fever	78
Cough	70
Weight loss	66
Dyspnoea	28
Diarrhea	10
Asymptomatic	2

Fever was hence the most common symptom (78%) at presentation followed by Cough (70%) in the study group.

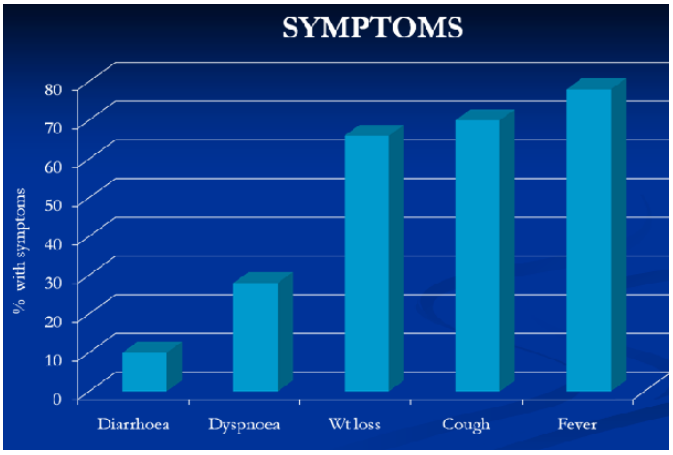

Fig 3: shows the frequency of symptoms in the study population

Opportunistic infections at presentation: The most common opportunistic infection at presentation was Candidiasis (76%) followed by Tuberculosis (54%). Meningeal tuberculosis was the most common form of Tuberculosis (14%).

Table 3: shows the incidence of opportunistic infections in the study group.

Opportunistic infection	Frequency (%)
Candidiasis	76
Tuberculosis	54
Meningeal	14
Pulmonary	12
Lymphadenitis	10
Disseminated	8
Pleural effusion	4
Miliary	2
Abdominal	2
Endometrial	2
Pneumocystis pneumonia	10
Cryptosporidium	6
Herpes	4
Cryptococcal meningitis	4

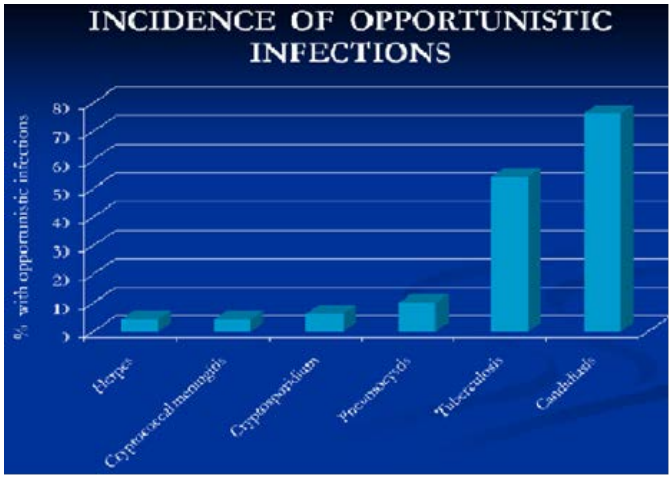

Fig 3: shows the incidence of opportunistic infections in the study group

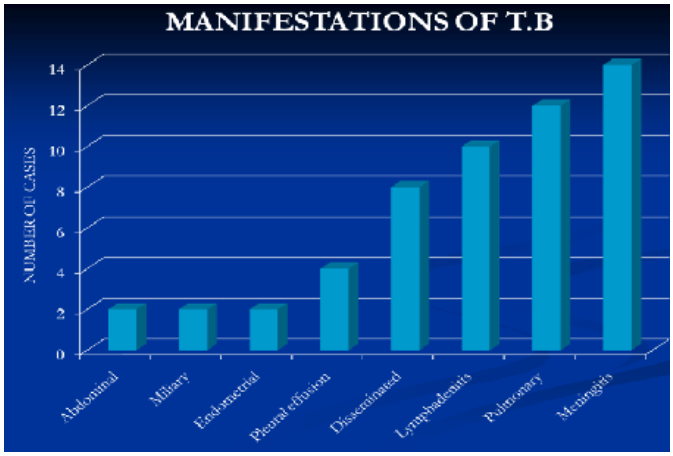

Fig 4: shows the frequency of manifestations of Tuberculosis

CD 4 count in the study group: The minimum CD 4 count among the individuals studied was 10 cells/µl whereas the maximum was 499 cells/µl with a mean value of 180 cells/µl. Majority of the patients had a CD 4 count of ≤ 200 cells/µl (64%).

Table 4: Shows the CD 4 count of the study group

	Minimum CD 4 count	Maximum CD4 count	Mean CD 4 count
CD 4 count	10.00	499.00	180.1600

Table 5: Shows the distribution of CD 4 count among the study population

CD 4 count	Frequency
< 200	64
200 – 400	24
≥ 400	12

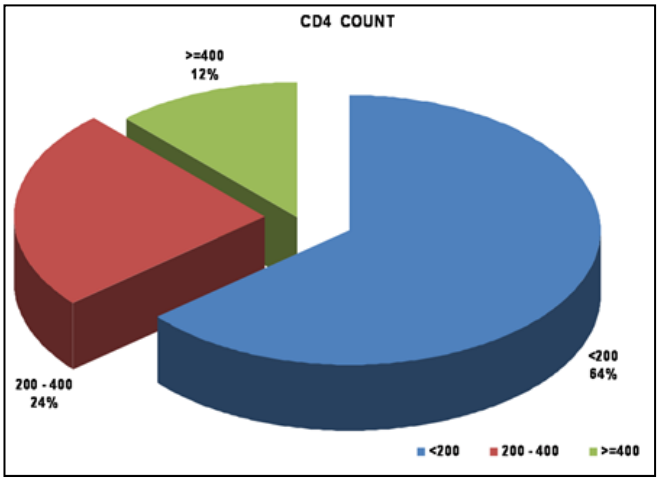

Fig 5: shows the distribution of CD 4 count among the study population

Correlation of age group with cd 4 count: Among the population studied, majority were in the 35 - 40 yr age group (28) out of which 21 individuals had a CD 4 count of < 200 cells/µl.

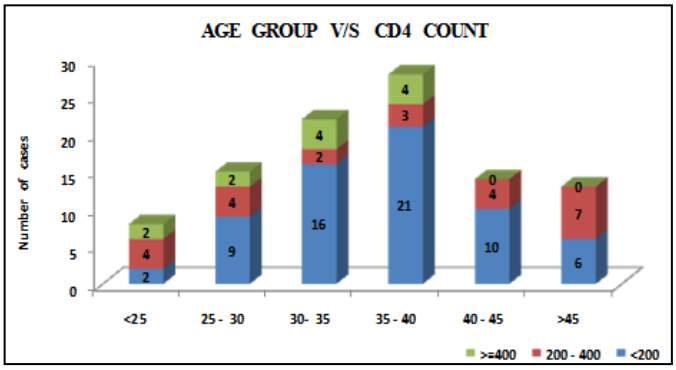

Fig 6: shows the correlation between age group and CD 4 count

Correlation between cd 4 count and opportunistic infections

The most common opportunistic infection in the study was Candidiasis which was seen in 76 patients out of which 62 had a CD 4 count of < 200. The second most common infection was Tuberculosis of which meningeal tuberculosis was the most common form. All 14 patients diagnosed to have meningeal tuberculosis had a CD 4 count of < 200. The majority of the cases of pulmonary tuberculosis occurred between a CD 4 count of 200 - 400 cells/µl. All the other extra pulmonary forms of tuberculosis occurred most frequently at a CD 4 count of < 200 cells/µl.

Table 6: showing the correlation of opportunistic infections Vs CD 4 count

Opportunistic infection	Total	CD4 <200	CD4 200 - 400	CD4 >400
Candida	76	62	14	-
Tuberculosis	54			
Meningeal		14	-	-
Pulmonary		2	8	2
Lymphadenitis		8	2	-
Disseminated		8	-	-
Pleural effusion		4	-	-
Miliary		2	-	-
Abdominal		2	-	-
Endometrial		2	-	-
Pnuemocystis	10	10	-	-
Cryptosporidium	6	4	2	-
Herpes	4	2	2	-
Cryptococcal	4	4	-	-

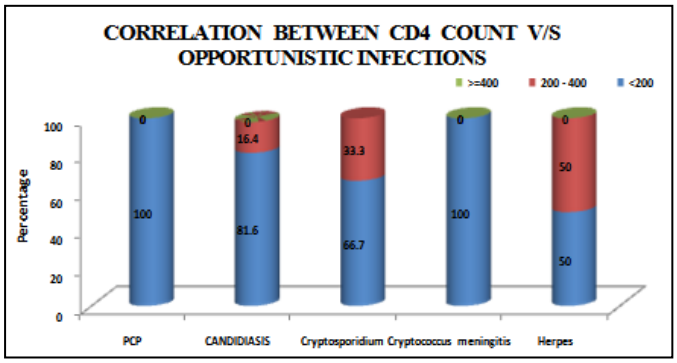

Fig 7: showing the correlation of opportunistic infections Vs CD 4 count

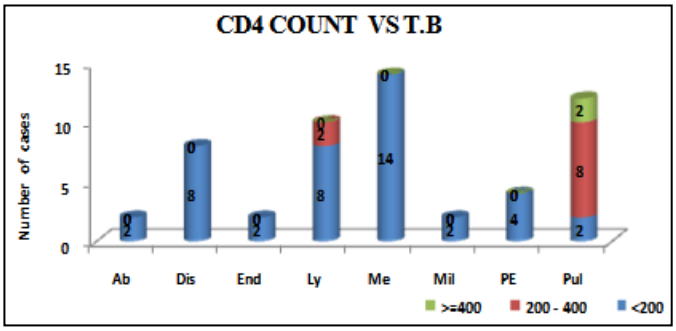

Fig 8: shows the correlation between CD 4 count and various forms of Tuberculosis

Discussion

Age

Majority of the patients in this study were in the age group between 35 - 40yrs (28%) with the mean age being 36.25 yrs. In a study of clinical profile of AIDS patients at a referral hospital, George J *et al.* [8] reported that the mean age of presentation was 30.3 +/- 6.4 yrs. In another study by Kothari K *et al.* [9], mean age at presentation was 32.76 +/- 8.14 yrs.

Sex

In this study, males accounted for 74% while females accounted for 26%. Other studies from India also show male predominance. George J *et al.* [8] reported male: female ratio of 5:1 in their study of AIDS patients in South India. Kumarasamy N *et al.* [10] reported a male to female ratio of 3.3:1. Male predominance could be attributed to social behavioral pattern of the population.

Mode of Transmission

This study showed heterosexual promiscuity as the major mode of transmission (99%). Only one case was attributed to vertical transmission. None of the patients acquired infection

by homosexual relationship or by blood transfusion. Similar mode of transmission was seen in other studies done in India. George J *et al.* [8] in their study of AIDS patients in South Indian reported that heterosexual transmission was the predominant mode of transmission (96.7%). Similar results were obtained in other studies also (Kothari K *et al.* [9], Kumarasamy N *et al.* [10]).

Symptom Analysis

In this study, fever was present in 78% of patients and cough was documented in 70% of patients. 66% patients had weight loss as the presenting symptom. Various other studies in India have described weight loss, fever and diarrhea as the most common presenting symptoms in HIV infected individuals. George J *et al.* [8] reported that fever was the commonest presentation (98.3%), followed by weight loss (85%) and cough (36.7%). Kothari K *et al.* [9] reported that fever was the presenting complaint in 96% patients. Only 2% patients were asymptomatic at presentation.

Opportunistic Infections

Candidiasis

In this study, oral candidiasis was the most common opportunistic infection. It was present in 76 out of 100 patients. The incidence of candidiasis in the study is comparable to that of other Indian studies. Data from Nagalingeswaran K *et al.* [11] showed that candidiasis was the commonest opportunistic infection with an incidence of 69.9%. However studies published by Kaur A *et al.* [12], George J *et al.* [8], Kumarasamy N *et al.* [10] and M. Vajpayee *et al.* [13] reported Tuberculosis as the most common opportunistic infection.

Significantly, candidiasis was present in 62 out of the 76 patients who had a CD 4 count < 200 cells/µl. Nagalingeswaran K [11] reported that oropharyngeal candidiasis occurred at a mean CD 4 count of 177 cells/µl. Data from M. Vajpayee *et al.* [13] showed that oral candidiasis occurred at a mean CD 4 count of 189 cells/µl.

Tuberculosis

In this study, Tuberculosis was the second most common opportunistic infection with 54 out of 100 patients having Tuberculosis. Of these, meningeal tuberculosis was the most common followed by pulmonary tuberculosis and tuberculous lymphadenitis.

Data from other observers in India show tuberculosis as the most common opportunistic infection in HIV in India. Kaur A *et al.* [12] reported that pulmonary tuberculosis was the commonest mode of presentation in their study concluded in Tamil Nadu, India. Numerous studies by George J *et al.* [8], Kumarasamy N *et al.* [10] and M. Vajpayee *et al.* [13] have shown tuberculosis as the most common opportunistic infection in AIDS.

Infection with tuberculosis was found in all subsets of CD 4+ T cell count. With CD 4+ T cell count more than 200 cells/µl, pulmonary involvement was the most common. However as CD 4 + T cell count fell below 200 cells/µl, incidence of extra pulmonary tuberculosis increased especially meningeal tuberculosis in this study.

Data from other studies confirm the observations made in the study. Nagalingeswaran K *et al.* [11] reported that pulmonary tuberculosis manifested itself at a mean CD 4 + count of 144 cells/µl, whereas increased incidence of disseminated tuberculosis was seen with a mean CD 4 + count of 125 cells/µl. M. Vajpayee *et al.* [13] also reported that pulmonary tuberculosis occurred at a CD 4 + count of 189 cells/µl and the incidence of extra pulmonary tuberculosis increased as the CD 4+ count decreased further.

Pneumocystis pneumonia

Pneumocystis pneumonia was observed in 10 patients in this study. Kothari K *et al.* [9] reported a 10% incidence of pneumocystis pneumonia in their study. Kumarasamy N *et al.* [10] reported an incidence of 4.6% whereas Nagalingeswaran K *et al.* [11] reported an incidence of 8.3%.

All the 10 patients in the study had CD 4+ count of < 200 cells/µl. Nagalingeswaran K *et al.* [11] observed that infection with Pneumocystis occurred at a CD 4+ count of 62 cells/µl. As the number of opportunistic infections in individuals increase, there is a significant increase in the mean viral load and decrease in the CD4 counts.

Cryptosporidium

In this study, cryptosporidium species was isolated in 6 patients. Kumarasamy N *et al.* [10] reported 16% incidence of cryptosporidial diarrhea. M. Vajpayee *et al.* [13] also reported 43.5% incidence of the infection. Four of the six patients had a CD 4+ count of < 200 cells/µl whereas two patients had a CD 4+ count between 200 – 400 cells/µl. Nagalingeswaran K *et al.* [11] reported that cryptosporidial diarrhea occurred at a CD 4+ count of 122 cells/µl whereas M. Vajpayee *et al.* [13] observed the occurrence of parasitic diarrhea at 227 cells/µl.

Herpes Zoster

In this study, 4 patients were diagnosed with this infection. Kumarasamy N *et al.* [10] reported an incidence of 7.3% of herpes zoster. Nagalingeswaran K *et al* [11] showed a 14.1% incidence. Two out the four patients had a CD 4+ count of < 200 cells/µl and the remaining had a CD 4+ count between 200 – 400 cells/µl. Nagalingeswaran K *et al.* [11] reported that herpes zoster occurred at a mean CD 4+ count of 248 cells/µl.

Cryptococcal Meningitis

Four of the patients presented with cryptococcal meningitis. The incidence is comparable to that of other Indian studies. Data from Kumarasamy N *et al.* [10] showed an incidence of 0.5% while Nagalingeswaran K *et al.* [11] reported an incidence of 1.9%.

All the patients diagnosed with cryptococcal meningitis had CD 4+ count <200 cells/µl. Nagalingeswaran K *et al.* [11] reported mean CD 4+ T cell count of 34 in patients with cryptococcal meningitis in their series.

Correlation between opportunistic infections and cd 4+ counts

In the natural course of HIV infection, with CD 4+ T cell count > 400 cells/µl, majority of the patients were asymptomatic. However, as the CD 4+ T cell count fell between 200 and 400, incidence of pulmonary tuberculosis, cryptosporidium and herpes zoster increased. Infections with

pneumocystis, cryptococcus and meningeal tuberculosis were seen exclusively with CD 4+ T cell count <200 cells/µl. This finding is in accordance with the data published by the Centre for Disease Control [14], Kumarasamy N *et al.* [10] and Nagalingeswaran K *et al* [11].

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