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Immune Reconstitution Inflammatory Syndrome in HIV positive patients on Anti-Retroviral therapy

KEYWORDS

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ABSTRACT Antiretroviral therapy has led to a significant decline in AIDS - associated morbidity and mortality (1). These benefits are in part a result of partial recovery of the immune system, manifested by increase in CD4 T-lymphocytes counts and decrease in plasma HIV-1 viral loads (2). In some patients, clinical deterioration occurs despite increased CD4 T-lymphocytes and decreased plasma HIV-1 viral loads (3). This clinical deterioration is due to inflammatory response of the immune system to both subclinical pathogens and residual antigens. Immune Reconstitution Inflammatory Syndrome (IRIS) is defined as a paradoxical deterioration in clinical status after initiating anti -retroviral therapy attributable to the recovery of the immune response to latent or subclinical infection or non-infectious processes. As we have very few Indian studies about IRIS, a study is planned to find the clinical spectrum of IRIS in HIV positive patients visiting a tertiary care center in Chennai

Aim :

To study the profile of Immune Reconstitution Inflammatory Syndrome in HIV positive patients on Anti-Retroviral therapy

Objectives :

Type of Opportunistic Infections

2. Correlation with the CD 4 count

MATERIALS AND METHODOLODY

This study is a **case control study** done on **HIV positive** patients on **Antiretroviral Therapy** at Government General Hospital at Chennai.

Immune Reconstitution Inflammatory Syndrome (IRIS) cases were diagnosed according to the latest **NACO guidelines**.

The **cases** included HIV positive patients who developed Immune Reconstitution Inflammatory Syndrome (IRIS) during Antiretroviral therapy (ART) and the **controls** included patients who did not develop IRIS during the ART.

Inclusion Criteria:

1). HIV positive patients on Anti-Retroviral therapy of age > 18yrs with an increase in CD4 count

2). Occurrence of opportunistic infection (New OI) or worsening of symptoms (Existing OI) within 6 weeks to 6 months after initiation of Antiretroviral therapy

Exclusion Criteria:

1). Patient not on Anti-Retroviral Therapy

2). Poor adherence

3). Defaulters

RESULTS AND ANALYSIS

This was a case control study where 40 IRIS cases were diagnosed in HIV positive patients on Antiretroviral therapy based on the NACO guidelines both retrospectively and prospectively which occurred between May 2008 to May 2010 and compared with 80 controls who were HIV positive patients on Antiretroviral therapy but did not develop IRIS.

The cases and controls were compared based on Age, Sex, Initial CD4 count, Final CD4 count, CD4 rise, Duration of ART, Type of ART and then the opportunistic infections and their relation to CD4 count was analyzed.

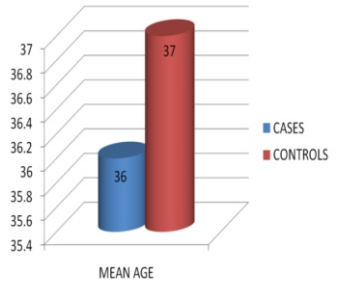

CHART 1 : AGE DISTRIBUTION

- The mean age of the cases is 36
- The mean age of the controls is 37

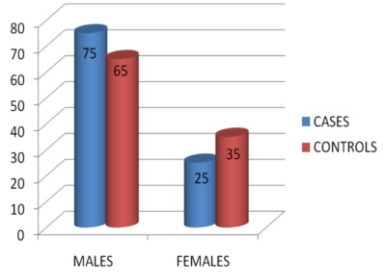

CHART 2 : SEX DISTRIBUTION

- In cases, 75% are males and 25% are females
- In controls, 65% are males and 35% are females

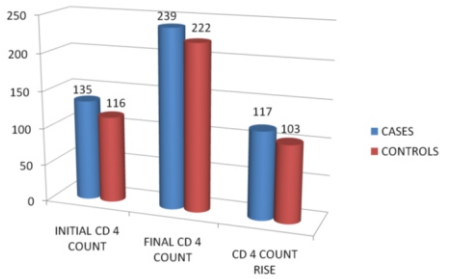

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CHART 3 : CD4 DISTRIBUTION

In cases, the mean initial CD4 count is 135
the mean final CD4 count is 239
the mean CD4 count rise is 117
In controls, the mean initial CD4 count is 116
the mean final CD4 count is 222
the mean CD4 count rise is 103

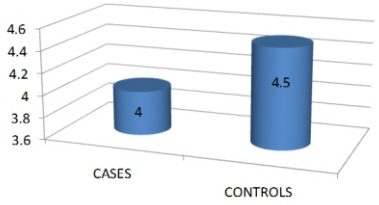


CHART 4 : MEAN DURATION OF ART

In cases the mean duration of ART was 4 months
In controls the mean duration of ART was 4.5 months

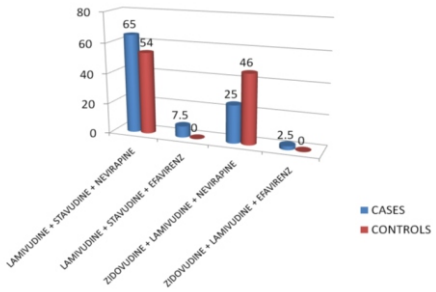


CHART 5: TYPE OF ART

In cases - 65% were on L+S+N regimen
25% were on Z+L+N regimen
7.5% were on L+S+E regimen
2.5% were on Z+L+E regimen
In controls - 54% were on L+S+N regimen
46% were on Z+L+N regimen

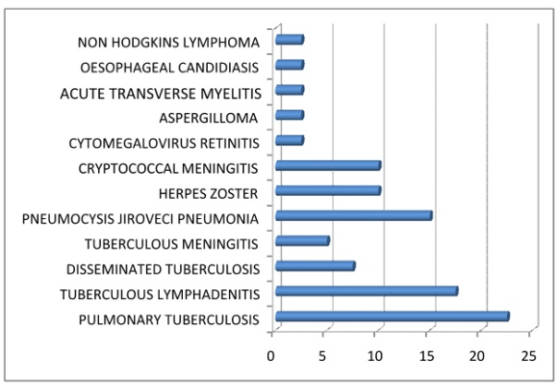


CHART 6: TYPE OF OPPORTUNISTIC INFECTION IN THE DIAGNOSED IRIS PATIENTS

22.5% with Pulmonary tuberculosis
17.5 with Tuberculous lymphadenitis
15% with Pneumocystis Jiroveci Pnuemonia
10% with Cryptococcal Meningitis
10% with Herpes Zoster
7.5% with Tuberculous Meningitis
5% with Disseminated Tuberculosis
2.5% with Cytomegalovirus retinitis, 2.5% with Oesophageal candidiasis, 2.5% with Aspergilloma, 2.5% with Non-Hodgkin's Lymphoma and 2.5% with Acute Transverse Myelitis

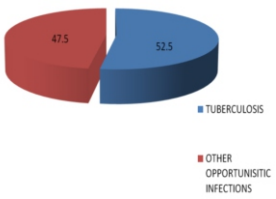


CHART 7 : TB IRIS AND OTHER OPPORTUNISTIC INFECTIONS

- 52.5% of the diagnosed IRIS patients had tuberculosis
- 47.5% constituted rest of all the opportunistic infections

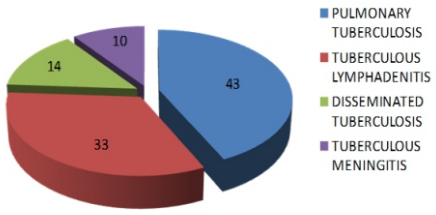


CHART 8 : SUBTYPES OF TB IRIS

- 43% with Pulmonary tuberculosis
- 33% with Tuberculous lymphadenitis
- 14% with Disseminated tuberculosis
- 10% with Tuberculous meningitis

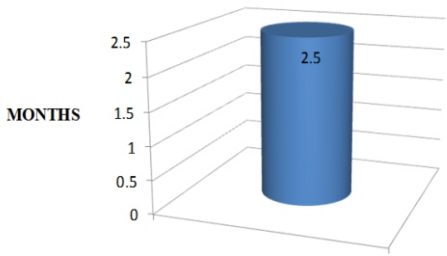
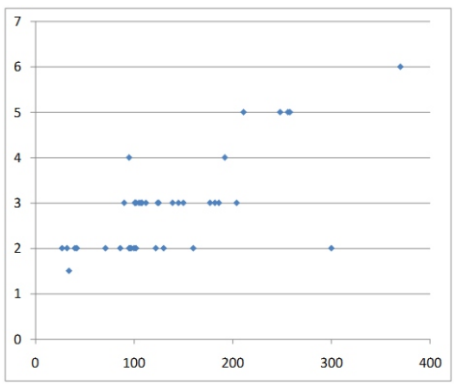


CHART 9 : MEAN DURATION BETWEEN ATT AND ART OF TB IRIS PATIENTS

- The mean duration between ATT and ART of TB IRIS patients is 2.5 months



DURATION OF ART IN MONTHS INITIAL CD4 COUNT

CHART 10 : CORRELATION BETWEEN INITIAL Cd4 COUNT AND THE DEVELOPMENT OF IRIS

- There is a weak correlation between the initial CD4 count and the development of IRIS

RESULTS :

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- The mean age of the IRIS patients was **36yrs.**
- **75%** of the patients were of **male sex** and the rest **25%** were of **female sex.**
- The mean **initial CD4 count** was **135.**
- The mean **final CD4** count was **239.**
- The mean **CD4 count rise** was **117.**
- The mean **duration of ART** in IRIS patients was **4 months.**
- **65%** of the IRIS patients were on **Lamivudine + Stavudine + Nevirapine Regimen**, 25% of them on Zidovudine + Lamivudine +Nevirapine regimen, 7.5% were on Lamivudine + Stavudine + Efavirenz and 2.5% were on Zidovudine + Lamivudine + Efavirenz.
- The most common opportunistic infection was the **Pulmonary Tuberculosis**, secondly **Tuberculous Lymphadenitis** and thirdly **Pneumocysitis Jiroveci Pneumonia.**
- **52.5%** of the IRIS patients had **Tuberculosis.**
- Among Tuberculosis patients **43%** of the patients had **Pulmonary Tuberculosis**, 33% of the patients had Tuberculous Lymphadenitis, 14% had Disseminated Tuberculosis and 10% had Tuberculous Meningitis.
- In TB IRIS patients the mean duration between ATT initiation and ART initiation was **2.5 months.**
- There is a **weak correlation** between initial CD4 count and the development of IRIS.
- There is a **weak correlation** between CD4 count rise and the development of IRIS.

DISCUSSION:

In this study a total of **40 cases** of HIV positive patients on ART who developed IRIS were identified and were matched with **80 controls** of HIV patients on ART who did not develop IRIS.

Following matching which was done for Age, Sex, CD4 count and Type of ART the opportunistic infections and their relationship to CD4 count was analyzed.

- In this study the most common opportunistic infection was **Mycobacterium Tuberculosis** followed by **Pneumocystis** infection. This is in accordance with the study by Narita M (8) where Mycobacterium Tuberculosis is the most common opportunistic infection in IRIS.

- In Tuberculosis, **Pulmonary tuberculosis** was the most common opportunistic infection, secondly **Tuberculous lymphadenitis** followed by **Disseminated Tuberculosis**. This is in accordance with the study done by Lawn SD (9) where pulmonary tuberculosis was the most common type of TB IRIS.

- TB IRIS occurred most commonly **2.5 months** after initiating ART. This is not in accordance with the Indian study done by Navas E (10) where most of the TB IRIS occurred within 2 months of initiating ART.

- There was weak correlation between a lower CD4 count or higher CD4 rise and the incidence of IRIS. This result was not in accordance from the study by Lenzo N, where there was a strong association between a lower CD4 count the development of IRIS.

CONCLUSION:

- In our study the most common opportunistic infection in Immune Reconstitution Inflammatory Syndrome in HIV positive patients on Antiretroviral therapy is **Mycobacterium Tuberculosis** followed by **Pneumocystis** infection.
- In Tuberculosis, **Pulmonary Tuberculosis** was the most common opportunistic infection followed by **Tuberculous lymphadenitis.**
- Here, TB IRIS most commonly occurred **2.5 months** after initiating of anti-retroviral therapy.
- There is a **weak correlation** between the a **lower CD4** count and the development of IRIS.
- There is a **weak correlation** between the **CD4 rise** and the development of IRIS.

LIMITATIONS:

- This is a small-scale study where only 40 diagnosed cases of IRIS are analyzed.
- The diagnosis of IRIS was based on only the rise in CD4 count and did not include a fall in HIV RNA levels.
- Drug Resistance to antiretroviral therapy was not ruled out.
- Drug Resistance opportunistic infection was not ruled out.

RECOMMENDATIONS:

- A large scale randomized controlled study is recommended.
- Diagnosis of IRIS should include a fall in the HIV RNA levels and a rise in CD4 count.
- Resistance testing to antiretroviral therapy should be done before a case is diagnosed as IRIS.
- Drug resistant opportunistic infection should be ruled out before diagnosing IRIS.

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