*ejpmr, 2018,5(10), 87-91*

SJIF Impact Factor 4.897

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

# CLINICOPATHOLOGICAL STUDY OF OPPORTUNISTIC INFECTIONS IN HIV POSITIVE CHILDREN WITH SPECIAL REFERENCE TO $CD_4$ CELL COUNT

**Dr. Shantisena Mishra[1], Dr. Pratibha Rai[2], Dr. Arakhita Swain*[3] and Dr. Saiprasanna Behera[4]**

[1]Associate Professor Dept. of Pediatrics, MKCG Medical College, Berhampur.
[2]Sr. Resident, Dept. of Pediatrics, SCB Medical College, Cuttack.
[3]Prof. Dept. of Pediatrics SLN Medical College, Koraput.
[4]Research Associate, Dept. of Pediatrics, SCB Medical College, Cuttack.

***Corresponding Author: Dr. Arakhita Swain**

Prof. Dept. of Pediatrics SLN Medical College, Koraput.

**Article Received on 15/08/2018** **Article Revised on 05/09/2018** **Article Accepted on 25/09/2018**

## ABSTRACT

**Background:** HIV in pediatric age group is a major world health problem. In India childhood, HIV amounts to around 4.4% of all cases. It is a large contributor to childhood morbidity and mortality in India. Usually the commonest cause of death in these children is opportunistic infections, which are more seen in $CD_4$ cell count depleted children. **Aims and Objectives:** The study was carried out with the objectives to find out the incidence of OI in HIV positive children and its relation to $CD_4$ cell count. **Materials and Methods:** Hospital based observational study conducted over on period of 2 years (Sept 2015 to Aug 2017) at pediatrics Dept. of SCB Medical College, Cuttack, India. HIV seropositive children less then 14 years of age were included in the study. Detailed clinical evaluation and lab investigations were done and they were put into WHO clinical stages. They were further classified based on $CD_4$ count. **Results:** Out of total 50 cases, 28 presented in stage-III and 15 in stage-IV at first visit. Girls had higher mean $CD_4$ count (488) than boys (340). PTB was most common OI (28%) followed by oral candidiasis. Children with OI had less $CD_4$ cell count. **Conclusion:** The clinical manifestations of HIV infection in children may be similar to number of other diseases. As the WHO clinical stage and grade of malnutrition increases, $CD_4$ count decreases thus can be a reliable marker of disease progression in HIV infected children.

**KEYWORDS:** HIV, $CD_4$ cell count, OI.

## BACKGROUND

HIV infection is becoming a prominent cause of childhood morbidity and mortality in India. Although children represent only 6% of all people infected with HIV/AIDS, out of this about 50% die within 2 yrs of onset, constituting about 18% out of the 3.2 million deaths due to HIV every year.[1]

The predominant mode of transmission in children is vertical i.e., it is acquired through intrauterine, intrapartum or through breast feeding from a HIV infected mother. Other routes such as sexual transmission and blood transfusion are not as common.[2]

Children with HIV infection differ from HIV infected adult patients. Children usually have higher viral load, weaker immune system, variable latency period, fewer opportunistic infections, fewer medicine approved for the management, different spectrum of clinical manifestations, diagnostic differences, and patterns of disease progression.

Soon after HIV was found to the cause of AIDS, it was shown that the virus binds to receptors on $CD_4$ cells, enters the cells and uses them to create new virus, destroying them in the process. This results in the depletion of $CD_4$ cells and immunodeficiency.

**Opportunistic infections (OIs)** are the most common cause of death among children living with HIV/AIDS. These infections are called "opportunistic" because they take advantage of the weakened immune system and they can cause devastating illnesses. OIs are a sign of declining immune system. OIs in children are usually primary and have a more fulminant course in comparison to adults. OIs in HIV children are typically seen in children with severe depression of $CD_4$ count or $CD_4$ %.[3]

With the increased availability of equipment to perform $CD_4$ counts and the knowledge that $CD_4$ cells were the primary target of HIV, the determination of $CD_4$ count became the standard measure of immunodeficiency in HIV infected patients in resource rich countries. The relative ease of $CD_4$ cell monitoring also led to its

advocacy in treatment guidelines for determining when to start, stop or change ART and for deciding when to initiate prophylaxis for opportunistic infections. This is despite the fact that $CD_4$ count does not always correlate with functional immunity; some patients with normal $CD_4$ counts are susceptible to OIs and some patients with significantly depressed $CD_4$ counts do not seem unduly susceptible to OIs. Hence this study attempts to correlate $CD_4$ count with opportunistic infections.

## AIMS AND OBJECTIVES

The present study was carried out with the objectives to find out the incidence and clinical profile of opportunities infections in HIV infected children less than 14 years of age and to correlate it with CD4 counts.

## MATERIALS AND METHODS

The study was a hospital based observational study conducted over a period of 2 years (Sept 2015 to Aug 2017) at Dept. of pediatrics, SCB medical college, Cuttack, India. Institutional ethics committee of the hospital approved the study. All children seropositive for HIV/DBS positive / whole blood DNA PCR positive below 14 years of age were selected as cases. Based on clinical presentations, they were classified into various WHO clinical stages who were further classified based on $CD_4$ counts according to WHO classification of immunodeficiency. Various data obtained were displayed in tables and charts, statistical analysis of the observations were done using percentages mean etc.

## RESULTS

In the study 30% of children were in the age group of 4 to 7 years. The mean age of presentation was 7.12 years. 56% of children presented with WHO clinical stage III & 30% with stage IV at first visit. Female children had higher mean $CD_4$ count (488 cells/cmm) than male children (340 cells/cmm). Vertical transmission was the predominant mode of transmission (92%). Anemia (48%), fever (42%) and cough (34%) were common symptoms. PTB (28%) was the most common opportunistic infection seen at mean $CD_4$ count of 267 ± 5.37, Oral candidiasis at $CD_4$ count of 364.8 ± 6.5, *Peneumocystis jiroveci* pneumonia at $CD_4$ count of 261.25 ± 0.8. Children with opportunistic infection had lesser $CD_4$ count. With the increasing grades of WHO clinical stage, there was $CD_4$ count decline, the severity of immune suppression increases with increasing WHO clinical stages.

## OBSERVATION

**Table 1: Age and Gender wise classification of Children.**

| Age group | Male (%) | Female (%) | Total (%) |
|---|---|---|---|
| 0 – 5Yr | 4 (14) | 7 (31) | 11 (22) |
| 5 – 7Yr | 6 (21) | 9 (41) | 15 (30) |
| 7 – 10Yr | 8(29) | 3 (14) | 11 (22) |
| 10 – 13 Yr | 10(36) | 3 (14) | 13 |

**Table 2: Age group and mean CD4 count.**

| Age group | Number (%) | Mean CD4 count ± SD |
|---|---|---|
| 0 – 5Yr | 11 (22) | 635 ± 11.49 |
| 5 – 7Yr | 15 (30) | 428 ± 9.61 |
| 7 – 10Yr | 11 (22) | 213 ± 8.13 |
| 10 – 13 Yr | 13 (26) | 209 ± 5.94 |
| Total | 50 (100) | |

**Table 3: Gender wise CD4 count of HIV infected children.**

| Gender | Number | Mean CD4 count ± SD |
|---|---|---|
| Male | 28 (56%) | 340 ± 8.31 |
| Female | 22 (44%) | 488 ± 9.63 |

**Table 4: Age and WHO classification of immunodeficiency.**

| Age group | No evidence of suppression | Evidence of moderate suppression | Severe suppression | Total |
|---|---|---|---|---|
| 0 – 5Yr | 2 (18%) | 5 (46%) | 4 (36%) | 11 |
| 5 – 7Yr | 4 (27%) | 4 (27%) | 7 (46%) | 15 |
| 7 – 10Yr | 3 (27%) | 3 (27%) | 5 (46%) | 11 |
| 10 – 13 Yr | 00 | 6 (46%) | 7 (54) | 13 |
| Total | 9 (18%) | 18 (36%) | 23 (46%) | 50 |

**Table 5: Frequency of various symptoms and sign in HIV infected children.**

| Symptoms and sign | Percentage |
|---|---|
| Fever | 42 |
| Recurrent / Chronic diarrhea | 7 |
| Cough | 34 |
| Weight loss | 25 |
| Skin lesions | 23 |
| Lymphadenopathy | 17 |
| Hepatomegaly | 7 |
| Hepatosplenomegaly | 3 |
| Anemia | 48 |
| Recurrent / persistent bacterial peneumonia | 10 |
| CNS involvement | 9 |

**Table 6: Opportunistic infections in HIV infected children.**

| Opportunistic infections | Percentage |
|---|---|
| Pulmonary tuberculosis | 26% |
| Abdominal Tuberculosis | 2% |
| Tubercular meningitis | 8% |
| Oral candidiasis | 10% |
| Pneumocystis carinii pneumonia | 8% |
| Herpes Zoster | 2% |

**Table 7: Correlation of CD4 count with opportunistic infection.**

| Opportunistic infections | Number (%) | Mean CD4 count ± SD |
|---|---|---|
| Abdominal TB | 1 (2%) | 348 |
| Pulmonary TB | 13 (26%) | 267 ± 5.37 |
| Oral candidasis | 5 (10%) | 364.8 ± 6.5 |
| Tubercular meningitis | 4 (8%) | 319 ± 3.36 |
| Pneumocystis Jirovecii pneumonia | 4 (8%) | 261.25 ± 10.8 |
| Herpes zoster | 1 (2%) | 613 |

**Table 8: Correlation of opportunistic infections with immunological category.**

| Opportunistic infections | No evidence of suppression | Evidence of moderate suppression | Severe suppression | Total |
|---|---|---|---|---|
| Abdominal TB | 0 | 1 (100%) | 0 | 1 |
| Pulmonary TB | 0 | 3 (20%) | 10 (80%) | 13 |
| Oral candidiasis | 0 | 2 (40%) | 3 (60%) | 5 |
| Tubercular meningitis | 0 | 2 (50%) | 2 (50%) | 4 |
| PCP | 0 | 0 | 4 (100%) | 4 |
| Herpes Zoster | 0 | 1 (100%) | 0 | 1 |

**Table 9: Correlation of CD4 count with WHO clinical stages.**

| WHO clinical stage | Number | Mean CD4 count ± SD |
|---|---|---|
| I | 4 | 1093 ± 10.73 |
| II | 3 | 611±8.85 |
| III | 27 | 338.5 ± 5.70 |
| IV | 16 | 307 ± 6.09 |

**Table 10: Correlation of WHO clinical stages with immunological category.**

| WHO clinical stage | No evidence of suppression (stage1) | Evidence of moderate suppression (stage 2) | Severe suppression (stage 3) |
|---|---|---|---|
| I | 5 (100%) | 00 | 00 |
| II | 3 (100%) | 00 | 00 |
| III | 1 (4%) | 13 (46%) | 14 (50%) |
| IV | 00 | 4 (29%) | 10 (71%) |

## DISCUSSION

Out of 50 cases in the study majority of children were in the age group of 4 to 7 years. The mean age of presentation was 7.12 yrs. Shah *et al* reported mean age of presentation of 4.7 years and study conducted by Ramesh R Pol reported mean age of 5.75 years and most of the children presented late with WHO clinical stage 3 (56%) and 4 (30%). In the present study, 28 (56%) were males and 22 (44%) were females. Male to female ratio was 1:0.78. Similar male predominance was noted in other studies like Agarwal et al[4], Shah et al[5] and Sehgal et al.[6]

It was observed that as age advances $CD_4$ count decreases. As the age advances severity of immune suppression increases and hence the $CD_4$ count decreases, however the statistical significance is not found using analysis of variance, [F = 1.01, p>0.05].

Female mean $CD_4$ count was 488 and for male it is 340, which is lower but the difference was statistically not significant. [t = 0.67, p > 0.05]. Similar result had been observed by Agarwal *et al.*[4]

Study showed that children with WHO clinical stage I had mean $CD_4$ count of 1093 ± 10.73 (8%), children with WHO clinical stage II had mean $CD_4$ count of 611 ± 8.85 (6%), children with WHO clinical stage III had mean $CD_4$ Count of 338.5 ± 5.70 (56%), children with WHO clinical stage IV had mean $CD_4$ count of 307 ± 6.09 (30%), which is in accordance with study conducted by Agarwal et al.[4] WHO clinical stages correlated with $CD_4$ count showed, as WHO clinical stage increases $CD_4$ count decreases. This was statistically also highly significant. F = 18.44, degrees of freedom = (3,46) and p < 0.01.

The most common presentation in the present study is Anemia (48%), followed by fever (42%), cough (34%), weight loss (25%), skin lesions (23%) in descending order, least being hepatosplenomegaly (3%). Higher incidence of anaemia, fever, cough and weight loss had also been observed in studies by Shah et al[5] and Agarwal et al.[4]

The study showed Tuberculosis (pulmonary and extrapulmonary) in 26% which is in accordance with study conducted by Ramesh. R Pol. (38.3%), Oral candidiasis in 12%, Pneumocystis carinii pneumoria in 8%, Molluscum Contagiosum in 6% & Herpc zoster in 7.14% which is in accordance with study conducted by Shah et al.[5]

Study showed opportunistic infections in 56% of children. Pulmonary TB was the most common opportunistic infection (26%) followed by oral candidasis (10%), Pneumocystis Jirovecii pneumonia was seen in 8% of children. Pulmonary TB was seen at mean $CD_4$ count of 267±5.37, Oral candidiasis was seen at mean $CD_4$ count of 364.8±6.5, *Pneumocystis Jirovecii* pneumonia was seen at mean $CD_4$ count of 261.25±10.8, tubercular meningitis was seen at mean $CD_4$ count of 319±3.36. Similar findings were observed in studies by Ramesh R Pol.[7]

The study showed Pulmonary Tuberculosis in 26% which is in accordance with study conducted by Agarwal et al (13.8%), Extrapulmonary Tuberculosis is seen in 10% of cases, which is in accordance with study conducted by Shah et al (10%).

The study showed all children with Pneumocystis jirovecii pneumonia, 80% of children with pulmonary TB and 60% of children with oral candidasis had evidence of severe immune suppression. Tubercular meningitis occurred with equal incidence (50%) with evidence of moderate suppression & severe suppression. Hence it is concluded that opportunistic infections increases with increasing immunological category.

The study showed, with the increasing WHO clinical stage there was decline of CD4 count. The mean CD4 count in WHO clinical stage I is 1093±10.73, II is 611±8.85. III is 338.5±5.70, IV is 307±09. This is also statistically significant F = 18.44, degrees of freedom = (3,46) and p < 0.01.

Study showed children with WHO clinical stage I and II had no evidence of immune suppression, children with stage III had evidence of moderate immune suppression in 46%, severe immune suppression in 50% of cases. Children with stage IV had evidence of moderate immune suppression in 29%, severe immune suppression in 71% of cases. The severity of immune suppression increases with increasing WHO clinical stages.

## CONCLUSION

Tuberculosis and oral candidiasis are the most common opportunistic infections in HIV infected children. Children with lower mean CD4 counts more likely to suffer from PCP and Pulmonary tuberculosis than other types of opportunistic infections. Perinatal transmission is the most common mode of acquiring HIV in Pediatric age group. As WHO clinical stage of HIV increases CD4 count decreases. CD4 count decreases as the grade of PEM increases. Besides ART, early diagnosis and prompt management of opportunistic infections still remains the cornerstone of HIV management and will definitely decreases the morbidity and mortality and increase the quality of life of those affected children.

## BIBLIOGRAPHY

1. Joint United Nations Program on HIV/AIDS (UNAIDS) WHO AIDS epidemic update 2012. Available from URL; http://www.unaids.org/en/resources/publications/2012/default.asp Accessed September 18, 2012.
2. Joint United Nations Program on HIV/AIDS (UNAIDS)/WHO AIDS epidemic update 2004. Available from URL;

http://www.unaids.org/en/resources/publications/2004/default.asp Accessed September 28, 2012.
3. Pediatric OI guidelines; from URL, http://aidsinfo.nih.gov/contentfiles/vguidelines/oi_guidelines_pediatrics.pdf. Accessed November 14, 2012.
4. Agarwal D, Chakravarty J, Sunder S, Gupta V, Bhatia BD. Correlation between clinical features and degree of immunosupression in HIV infected children. Indian Pediatr, 2008; 45: p140-43.
5. Shilpa R, Shah, Milind S, Tullu, Jaishree R Kamat. Clinical profile of pediatric HIV infectio from India. Archives of Medical research, 2005; 36: p24-31.
6. Sehgal R, Baveja UK, Chattopadhya D, Chandra J, Lal S. Clinical profile of HIV infection in children in north India. Indian J Pediatr, 2005; 72(11): 925-30.
7. Pol RR, ShepurTA, Ratageri VH. Clinico-Laboratory Profile of pediatric HIV in Karnataka. Indian J Pediatr, 2007; 74(12): 1071-5.