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Original Research Article

A study of clinico-immunological response to art in HIV infected children in western Rajasthan

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ABSTRACT

Background: Study of clinico immunological response to antiretroviral drugs in HIV infected children.
Methods: 50 HIV positive children after immunological categorization put on first line pediatric ART treatment according to pediatric ART NACO guideline, side effect, clinical response (in the form of change of WHO clinical staging), and immunological response (in the form of change of CD4 count, and immunological staging) were noted on follow up study.
Results: The Correlation between WHO clinical staging and immunological staging was poor so initiating anti retro viral treatment should be preferably based on CD4 count. Children who were initiated on ART have a significant improvement in both WHO clinical and immunological staging at the six and twelve months follow up and ART found to be well tolerated.
Conclusions: Significant clinical and immunological improvement occur in the children who were put on ART based on CD4 counts provided if the adherence level is very good.

Keywords: Adherence, ART therapy, Immune response, Pediatric HIV

INTRODUCTION

AIDS is a global pandemic and infected tens of millions in <20 years periods.[1] Children are becoming the innocent victim of this dreadful disease.

Each day 11000 persons are infected globally out of those 1800 cases are pediatric populations. In India 200 cases detected daily out of those four from Rajasthan.[2-5] In year 2015 2117000 peoples are living with AIDS in India. AIDS cases till March 2005 in Rajasthan come to about 88560. Rajasthan with an official Sero-prevalence of 0.5 percent can be described as a highly vulnerable, high-priority state.[5] HIV infection progress faster in children and has fatal out-come. This is correlated with higher viral burden and faster cd4 lymphocyte depletion.[6,7]

The present study is therefore under taken to evaluate immunological behaviour of HIV infected children at first time attending our ART centre, during pre-ART phase, and after giving the ART and to find out clinical and immunological response to anti retro viral treatment.

METHODS

This observational prospective study conducted in the Umaid hospital and attached ART centre for one year and follow up done after six and twelve months.

Patients were diagnosed as per NACO guide line and classified according to WHO clinical staging guideline. ART started after immunological classification and age specific CD4 cut off value was as following:

Pts <11 months if CD4 <25% (<1500 cells/mm^3), 12 - 35 months if CD4 <20% (<750 cells/mm^3), 36-59 months if CD4 <15% (<350 cells/ mm^3) and patients >5 years old if CD4 counts <350 cells/mm^3 especially if symptomatic, initiate ART before CD4 drops below 200 cells/ mm^3 and WHO Clinical staging 3 and 4 irrespective of CD4 counting as per slandered protocol.

After clinical, immunological staging, 50 HIV positive children treated according to pediatric ART NACO guideline by first line fixed dose combination Pediatric treatment regimen like Regimen P1, Regimen P1A, Regimen P2, and Regimen P2A

Regimen P1 is comprise of Zidovudine + Lamivudine +Nevirapine preferred first line regime except for those patients who are anemic (Hb < 9 gm%). REGIMEN P1A encompasses Stavudine +Lamivudine + Navirapine as a first line regime for those patient in which Hb was less than 9 gm%. REGIMEN P2 contains Zidovudine + Lamivudine and Efavirange and this regime was used in those children who are on ATT (anti tubercular treatment), weight >10 kg, and Hg >9 gm%. REGIMEN P2A contains Stavudine + Lamivudine and Efavirenge and this regime is used in those children who were on ATT (anti tubercular treatment), weight >10 kg, and Hg <9 gm%.

All these regimes were supplied as pediatric FDC (fixed dose combination), dual or triple combination.

All children were visited every month for follow up for clinical evaluation, weight gain, CD4 count (6 monthly), side effect, clinical response (in the form of change of WHO clinical staging), and immunological response (in the form of change of CD4 count, and immunological staging) were noted.

RESULTS

In present study, all 50 patients started with first line ART regimen, 30% were received P1, 24% child were received p1a, 24% child were received P2, and 22% child were received P2a regimen.

Table 1: Mean SD and CD4 count at presentation and follow up of art patients.

At presentation			At follow up		
Clinical stage	No. of pt.	CD4 pre-Mean (SD)	CD4 FU Mean (SD)	Change CD4 mean (SD)	P value
Stage-I	00	Na	Na	Na	Na
Stage-II	12	181.00 SD 27.65	295.00 SD 65.11	114.00 SD 37.46	<0.001
Stage-III	26	221.19 SD 80.88	351.11 SD n124.65	129.92 SD 43.77	<0.001
Stage-IV	12	291.75 SD261.03	410.00 SD 228.03	118.28 SD 33.00	>0.03

Children who were initiated on ART have a significant improvement in their CD4 count and WHO clinical staging at first follow up.

Table 2: Mean SD and CD4 count at presentation and follow up of art patients.

At presentation			At first follow up		
Immune stage	No of pt	CD4 pre-Mean (SD)	CD4 FU Mean (SD)	Change CD4 Mean (SD)	P value
Stage I	00	NA	NA	NA	NA
Stage II	12	326.41 SD 227.91	409.08 SD 112.41	82.67 SD 115.5	<0.3
Stage III	38	197.55 SD86.23	333.68 SD155.58	136.13 SD 69.35	<0.001

Children who were initiated on ART have a significant improvement in their CD4 count and WHO immune staging at first follow up.

Table 3: Distribution of art cases according to CD4 response from art.

1st FU CD4	No of Pt	Level of adherence	2nd FU CD4	No. of pt	Level of adherence
Increased	45	A (30), B (15)	Increased	41	A (30), B (11)
Decreased	02	C (1), D (1)	Decreased	04	C (1), D (3)
No change	03	C (2), (1)	No change	05	C (2), D (3)

In present study out of 50 cases, IRIS phenomena (Immune Reconstitution Inflammatory Syndrome) was seen in 07 cases (14%).

Out of 50 patients, 27 children were used Zidouvidine based regimen, 3children (11.11%) developed anaemia, one child (3.7%) developed neutropenia, two children (7.40%) severe G.I. intolerance, and 20 children (74.07%) developed mild GI intolerance.

Out of 50 patients, 23 children were used Efavirange based regimen, 4 children (17%) developed skin rashes. In present study 27 children were treated with Zidovudine based regimen, among them 6 (22.22%) children

switched to Stavudine based regimen, three (11.11%) children due to development of anaemia (Hb<7.5), two (7.4%) child due to persistence G.I. intolerance, and one (3.7%) children due to neutropenia. In present study out of 50 patients, 12 (24%) child was on clinical stage II, at first follow up have higher mean CD4 (295.00) as compare to their initial presentation (181.00) and 26 children with clinical stage III, at first follow up have higher mean CD4 (351.11) as compare to their initial presentation (221.19). This is statistically significant (P <0.001). On the contrary 12 patients of clinical stage IV, at their first follow up have higher mean CD4 (410.00) as compare to their first-time presentation with mean CD4 (291.75) but this was statistically not significant (P >0.03) Table 1.

In present study out of 50 patients, 12 children were on immunological stage II, have higher mean CD4 (409.08) at their first follow up as compare to their baseline mean CD4 (326.4) but this difference was not found significant. (P <0.3) but on second follow up the mean CD4 (586.08) significantly increased as compare to their first follow up (P <0.01). whereas in 38 (76%) children who were in immune stage III, had higher mean CD4 (333.68) on follow up as compare to their baseline mean CD4 (197.55) at the time of presentation this was found statistically significant (P < 0.001) Table 2.

In present study 50 patient on ART first follow up show that 45 out of 50 had increased CD4 count, 30 of these patients has >95% level of adherence, 15 patient had b/w 85 to 95%, 5 patients had no change or decreased CD4 response having level of adherence either <85% or not measurable. whereas on their second follow up visit depicted that 41 out of total 50 had increased CD4 count, 30 of these patients has >95% level of adherence, 11 patient had b/w 85 to 95%, 9 patients had no change or decreased CD4 response having level of adherence either <85% or not measurable. This was found statistically significant. (P < 0.001) Table 3.

ART patients whose level of adherence was more than 85% to 95% or more they also had significant improvement in the clinical staging and immunological staging the form of increased CD4 counts (Table 4, Table 5).

Table 4: Comparison of art cases according to clinical staging at the time of presentation and on follow up.

Who clinical staging	At time of presentation	At 1st follow up	At 2nd follow up
I	00	12 (24%)	25 (50%)
II	12 (24%)	23 (46%)	20 (40%)
III	26 (52%)	13 (26%)	05 (10%)
IV	12 (24%)	02 (04%)	00

Children who were initiated on ART has a significant improvement in both WHO clinical staging at the six months and twelve-month follow-up.

Table 5: Comparison of art cases according to mean immunological staging at the time of presentation and follow up.

CDC immunological staging	At time of presentation	At 1st follow up	At 2nd follow up
No suppuration (stage I)	00	02	11
Modrate suppration stage II	13	37	31
Severe suppration stage III	37	11	08

Children who were initiated on ART have a significant improvement in immunological staging at both six months and twelve-month follow-up.

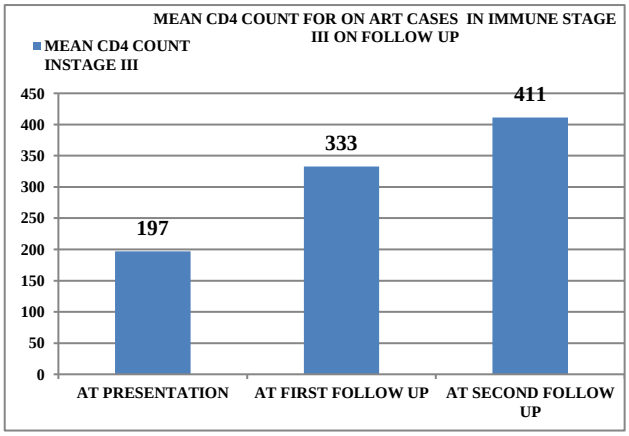

Figure 1: Mean CD4 count for on art cases in immune stage iii on follow up study (p <0.05).

DISCUSSION

In our study in ART group with WHO clinical staging II there were 83.33% cases in severe immunosuppression, with clinical stage IV there were only 66.66% were in severely immunosuppresed at the time of presentation.

In our study, all ON ART group 50 patients started with first line ART regimen, 30% were received p1(Zidovudine + Lamivudine + Nevirapine), 24% child were received p1a (Stavudine + Lamivudine + Nevirapine), 24% child were received p2(Zidovudine + Lamivudine + Efavirenz), and 22% child were received p2a (Stavudine + Lamivudine + Efavirenz) regimen according to NACO guideline. In present study out of 50 cases, received ART regime first time, IRIS phenomena (Immune Reconstitution Inflammatory Syndrome) developed in 07 cases (14%). Immune reconstitution inflammatory syndrome (also known as "Immune recovery syndrome" is a condition seen in some cases of AIDS or immunosuppression, in which the immune system begins to recover, but then responds to a previously acquired opportunistic infection with an

overwhelming inflammatory response that paradoxically makes the symptoms of infection worse. [8,9]

The suppression of CD4 T cells by HIV (or by immunosuppressive drugs) causes a decrease in the body's normal response to certain infections.[10] Not only does this make it more difficult to fight the infection; it may mean that a level of infection that would normally produce symptoms is instead undetected (subclinical infection). If the CD4 count rapidly increases (due to effective treatment of HIV, or removal of other causes of immunosuppression), a sudden increase in the inflammatory response produces nonspecific symptoms such as fever, and in some cases a worsening of damage to the infected tissue.

In present study mean CD4 count decreased in Pre-ART cases during follow up, and mean CD4 count increased in who were started with ART. The ART patients whose level of adherence was more than 85% to 95% or more they also had significant clinical improvement in the form of weight gain, already existing opportunistic infection improved, working efficiency improved, clinical staging improved, and immunological staging improved in the form of increased CD4 counts similar type of observation are also reported from the study of Gomber et al, and other Indian studies which denotes the clear cut benefits of ART adherence and counseling.[7]

Limitations of our study include long term follow up is required to further know the fate and outcome of the children who started on ART

CONCLUSION

The Correlation between WHO clinical staging and immunological staging was poor so initiating anti retro viral treatment should be preferably based on CD4 count where the facility is available. Children who were initiated on ART have a significant improvement in both WHO clinical and immunological staging at the six and twelve months follow up and ART found to be well tolerated. Significant clinical and immunological improvement observed in the children who were put on ART provided if the adherence level is very good.

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