IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 14, Issue 12 Ver. I (Dec. 2015), PP 50-57
www.iosrjournals.org

Study Of Prevalence Of Malnutrition In HIV Positive Children And Its Correlation With Cd4 Count

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Abstract:
Background: *Malnutrition goes hand in hand with immunosuppressed children. There are few studies describing the prevalence and determinants of malnutrition among children with HIV/AIDS in India.*
Aim: *The present study is to determine the prevalence of malnutrition in HIV positive children in the age group of 0 – 5 yrs in tertiary care center and to correlate the immune status with malnutrition in these children.*
Material and Methods: *From 2011 to 2012, we conducted a cross-sectional study among 213 ART-treated HIV-positive children in the age group of 0-5 years who were referred to Niloufer Institute for women and child health, India. We measured the children's anthropometrics, socio-demographic factors, food security, dietary habits, diarrhea episodes, economic status, and HIV clinical stage. Data were analyzed using both univariate and multivariate methods.*
Results: *In this cohort, the prevalence of underweight (WAZ <-2SD) was 61 %(n=130), stunting (HAZ<-2SD) was 56.8 %(n=121) and wasting (WHZ<-2SD) was 29.2 %(n=62) respectively.We examined the relationship between CD4% and the various growth parameters. We found that 34.27% (n=73) of the children were severely immunosupressed (CD4 %< 15%).Of these children with CD4<15%, 75.34% were underweight and 64.38% were stunted.36.98% of children among these group were wasted. In our cohort we have found that 90% of the underweight and wasted children have moderate to severe immunosuppression (CD4% <=25%).Around 85% of the stunted children were having moderate to severe immunosuppression. Higher rates of moderate to severe stunting, underweight and wasting were observed among children with CD4 <15% compared to those at higher CD4%. There was a low or weak correlation between underweight and CD4% ($p<0.05$, $r=0.24$) and between wasting and CD4% ($p<0.05$, $r=0.13$).*
Conclusions: *In summary, we have found that malnutrition (both stunting and underweight) is highly prevalent among HIV- infected children in India. Growth failure cannot be used as a surrogate marker to stage HIV disease as it occurs even at relatively higher CD4 levels. Malnutrition should be targeted early to ensure optimal response to ART and reduce early mortality. Future studies should also examine the impact of nutritional supplementation started at different stages of HIV disease on reducing HIV-related mortality and morbidity in children and in modifying long-term treatment outcomes.*
Keywords: *HIV, children, malnutrition, CD4 counts*

I. Introduction

Nutrition and HIV are closely interlinked creating a vicious cycle. Even at the early stage of HIV when the effects may not be visible (asymptomatic phase), HIV infection has a substantial impact on the nutritional status of infected people due to poor food intake as a result of poor appetite and difficulty eating, intestinal malabsorption because of chronic diarrhea and HIV caused intestinal cell damage, metabolic changes and increased nutrient requirements related to opportunistic infections (OIs) (1). In turn malnutrition can further weak the immune system and worse the effects of the HIV-disease and related OIs. Good nutrition does not cure AIDS or prevent HIV infection, but it could break this vicious cycle and improve the health and the life-quality of people living with HIV/AIDS, by maintaining body weight and strength, replacing losses of vitamins and minerals, improving the function of the immune system and the body's ability to fight infection, extending the period of infection to development of the AIDS-disease, improving response to treatment, reducing time and money spent on health care and then keeping HIV-infected people active and productive (2).

The inter-dependence between nutrition and resistance to infection has been substantiated by pertinent observations, epidemiological data and research. Growth failure in children is more common in HIV infected

children. WHO recommends a 10% increase in energy intake for asymptomatic HIV-infected children, with further increase of 20– 30% and 50–100% for those children who are symptomatic and experiencing weight loss respectively (24).

CD4 cells or T cells are lymphocytes and are responsible for the human immune system. Of these CD4 + are 'helper cells' which lead the attack in infections and CD8 + are 'suppressor cells' that end immune response. In HIV infection the CD4 and CD8 cell counts go down indicating immune damage. Protein–energy / calorie malnutrition (PEM) is the commonest cause of immuno-deficiency. PEM has been associated with lowered CMI as indicated by reduced number of CD4 T cells, lower CD4 : CD8 ratios, LPR to mitogens, , impairment of phagocytic functions and secretory IgA (1). Dr Narayan advised that periodic estimates of CD4 rather than a single count is more reliable and useful for understanding the impact of the disease (3).

II. Materials And Methods

DESIGN: A hospital based cross sectional study.

SETTING: Niloufer Institute for women and child health, Osmania Medical College in Hyderabad,Telangana, India.

PARTICIPANTS: A total of 213 HIV positive children in the age group of 0 - 5 yrs, who are referred to ART center at Niloufer Hospital.

STUDY PERIOD: January 2011 – May 2012.

INCLUSION CRITERIA:

1. Children between the age group of 0 - 5 yrs with HIV positivity (4) referred to ART centre.
2. Both male and female children.
3. Parents or guardians who gave consent for their children.

EXCLUSION CRITERIA:

1. Children aged above 5 yrs.
2. Children who are already on ART.
3. Children who are on nutritional supplementation.
4. Children who are in clinical stage 4 HIV.

Methods:

Ethical committee review and approval was taken from Osmania medical college, Hyderabad. All consecutive HIV positive children between the age group of 0-5 yrs who were referred to ART centre were enrolled in the study after their parents or guardians consent. Parents socioeconomic status was graded according to the recent Kuppuswamy's socioeconomic scale from class 1 to class 5 (5). Brief history and clinical examination along with anthropometric measurements were taken. Preterm children were defined and counted as children born with gestational age less than 37 completed weeks and Term as 37 to < 42 weeks of gestation. Appropriately immunized children were defined as those who had taken all the vaccines at an appropriate age according to IAP immunization schedule. These children were classified according to WHO clinical staging from stage 1 to stage 4 (6).

Weight was measured through a standard weighing machine with zero error in kilograms and height/length was taken on a standard stadiometer (for children above 2 years) and infantometer (for children below 2 years) in centimeters. Three anthropometric indices were computed and expressed as standard deviation units from the median for the international reference population. Deviations of the indicators below –2 SD indicate that the children are moderately affected, while deviations below –3 SD indicate severely affected. Grading of malnutrition was done as underweight (low weight for age), stunting (low height for age) and wasting (low weight for height) according to the WHO guidelines (7).

The immune classification is based on the absolute CD4 lymphocyte count or the percentage of CD4 cells. Age adjustment of the absolute CD4 count is necessary because counts that are relatively high in normal infants which decline steadily until 6 yr of age, when they reach adult norms. No evidence of suppression when cd4 % ≥ 25, moderate suppression when cd4% is 15-24, severe suppression when cd4% is <15 (8). CD4 count and CD4 percentage were measured by standard flow cytometric methods using the Beckman Coulter Epics XL.

Data Analysis:

A master chart of Microsoft Excel 2007 version was prepared with all the data collected from the study. Observation and tables was made in a statistical form from the clinical data available. For all the statistical analysis SPSS statistical software, version 19.0 for windows (SPSS Inc, Chicago, IL, USA) was used. Chi square test was done for statistical significance. In all instances a p value ≤ 0.05 was considered statistically significant. Those parameters which showed significance were subjected to regression analysis and a correlation factor (r) was calculated. If r value was ≤ 0.35 we considered low or weak correlation, 0.36 to 0.67 to be modest or moderate correlation, 0.68 to 1.0 as strong or high correlation and ≥0.90 as very high correlation.

III. Results

In our study a total of 213 antiretroviral naïve HIV-infected children (100%) were included and the data was analyzed. There were 106 males (49.77%) and 107 females (50.23%) with a mean age of 36.32 months ±18.934 (Range = 4months to 60months).

In total population the class 1 socioeconomic status is seen in 1 (0.5%), 11(5.2%) children belongs to class 2, 52(24.4%) children belongs to class 3, 122(57.3%) children belongs to class 4, 27(12.7%) children belongs to class 5 (Fig 1).

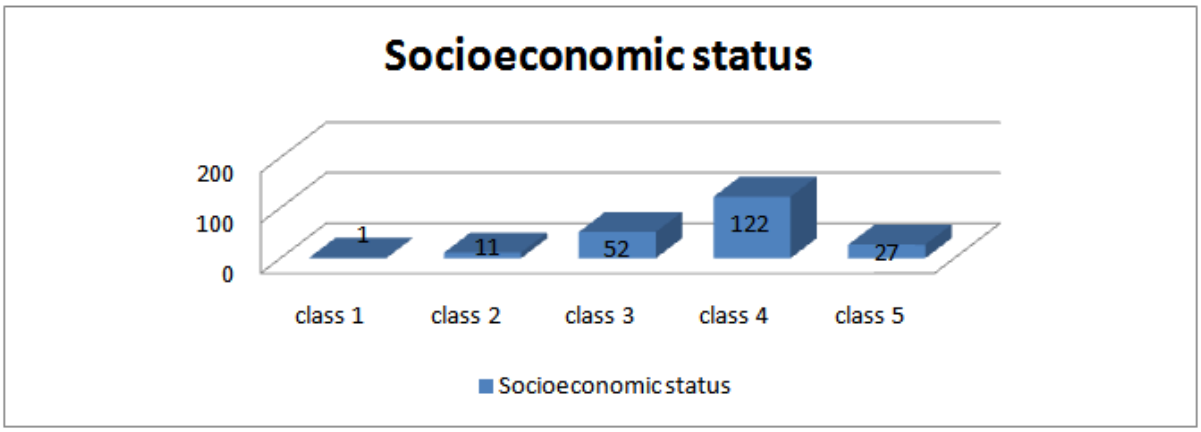

Fig 1: Socioeconomic status based on Kuppuswamy scale

Most of the children acquired HIV infection through mother to child transmission (n=208) 97.7% and 0.9% (n=2) of children acquired the disease via blood transfusion. In three children (1.4%) the mode of transmission is unknown (Fig 2).

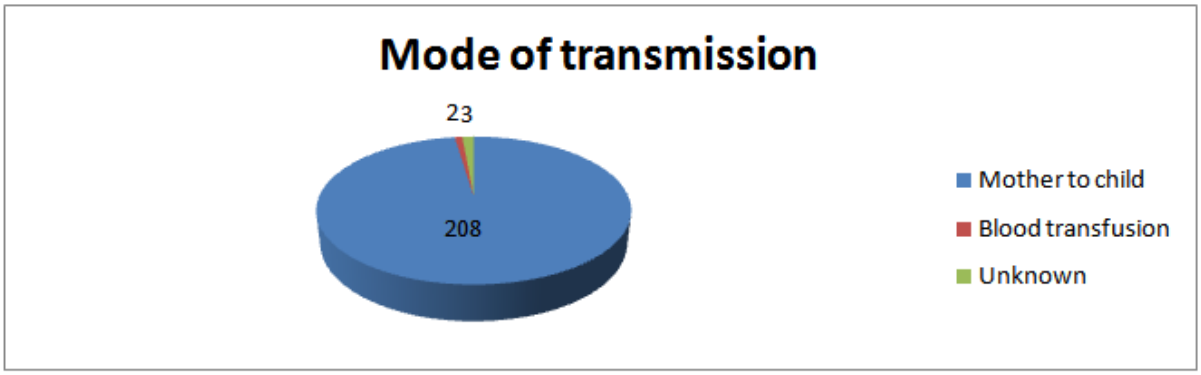

Fig 2: Mode of transmission in children

In our study 72.8% of the children were in WHO clinical stage 2 (n=155), 16.9% of the children were in stage 3 (n=36) and 10.3% of the children were in stage 1 (n=22) (Fig 3).

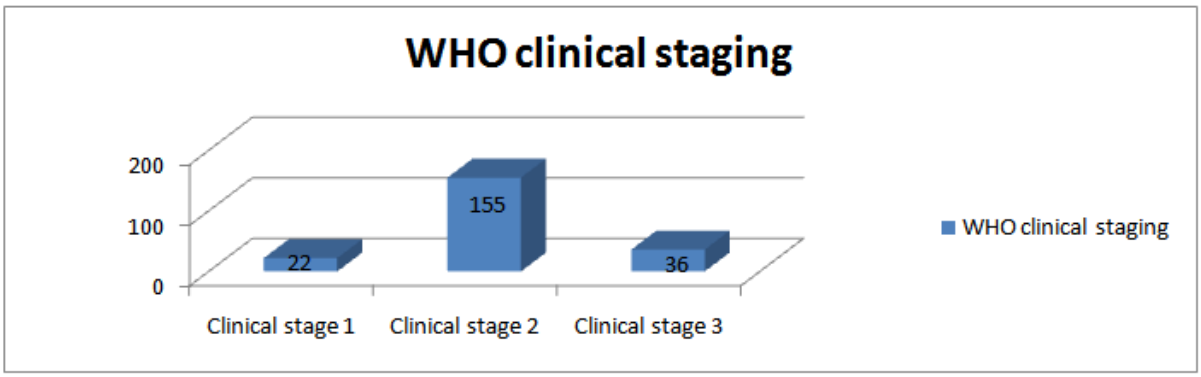

Fig 3: WHO clinical staging 1-3 of the study population

In our study we have found out that 34.27 %(n=73) of children had severe immunosupression (CD4% <15%), 48.35% (n=103) children had moderate immunosupression (CD4% 15-24%) and 17.37 %(n=37) children had no immunosupression (CD4% ≥ 25%) (Fig 4).

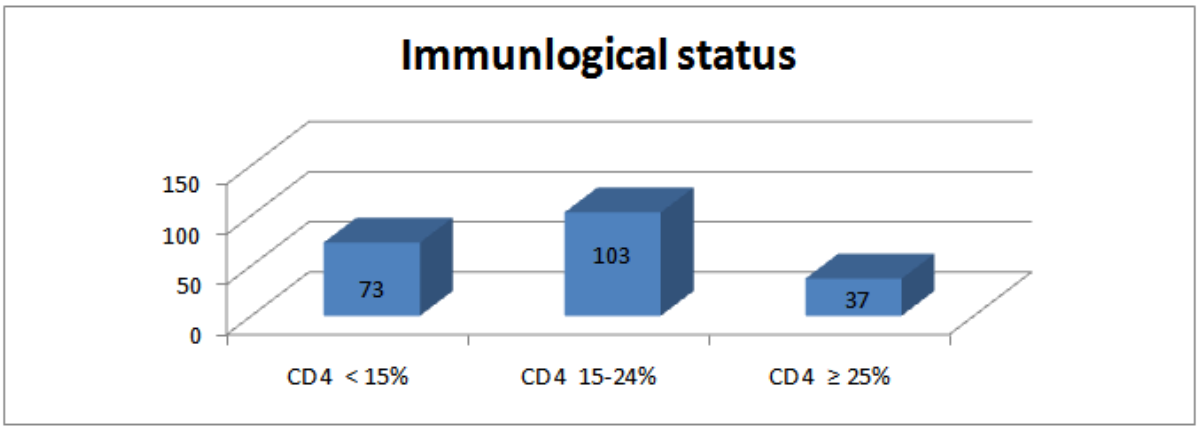

Fig 4: Immunologic status of the study group

In our study we have found that 65.3% (n=139) of the children were appropriately immunized and 34.7% (n=74) were inappropriately immunized. We have found that 210 (98.6%) children were staying with their parents and 3 children (1.4%) were staying in hostels. 198 (93%) were born at term gestation and 15 (7%) were preterm's.

The Mean birth weight of the study group of children was 2.53 ± 0.468 kgs. The mean duration of breast feeding was 8.8 ± 7.76 months. The mean weight was 10.12 ± 3.35 kgs and the mean height was 82.99 ± 13.88 cms. The mean CD4 count was 889.25 ± 662.48 cells /cumm. The mean CD4% was 17.99 ± 8.03 (Table 1) (Table 2).

	N	Minimum	Maximum	Mean	Std. Deviation
Age (months)	213	4	60	36.32	18.934
Birth weight (kg)	213	1.0000	4.0000	2.538826	.4683432
Breast fed till (months)	213	.0	36.0	8.800	7.7605
weight (kg)	213	3.5	19.0	10.125	3.3504
height(cm)	213	46.0	112.0	82.986	13.8817
CD4count	213	18	3492	889.25	662.481
CD4 %	213	1	44	17.99	8.026
Valid N (listwise)	213				

Table 1: Demographic profile of the study population

Sex		N	Minimum	Maximum	Mean	Std. Deviation
Male	Age (months)	106	4	60	35.06	19.060
	Birth weight (kg)	106	1.0000	4.0000	2.538113	.4972077
	Breast fed till (months)	106	.0	36.0	8.632	8.0644
	weight (kg)	106	3.5	19.0	9.995	3.2245
	height(cm)	106	46.0	112.0	82.797	13.7090
	CD4count	106	18	3410	953.71	691.285
	CD4 %	106	1	40	17.29	7.902
	Valid N (listwise)	106				
Female	Age (months)	107	4	60	37.58	18.813
	Birth weight (kg)	107	2.0000	3.5000	2.539533	.4402345
	Breast fed till (months)	107	1.0	36.0	8.967	7.4815
	weight (kg)	107	5.0	18.0	10.254	3.4810
	height(cm)	107	46.0	110.0	83.173	14.1128
	CD4count	107	66	3492	825.39	629.385
	CD4 %	107	3	44	18.67	8.126
	Valid N (listwise)	107				

Table 2: Demographic profile of the study population in both sexes

In this cohort, the prevalence of underweight (WAZ <-2SD) was 61 %(n=130), stunting (HAZ<-2SD) was 56.8 %(n=121) and wasting (WHZ<-2SD) was 29.2 %(n=62) respectively (Fig 5) (Table 3).

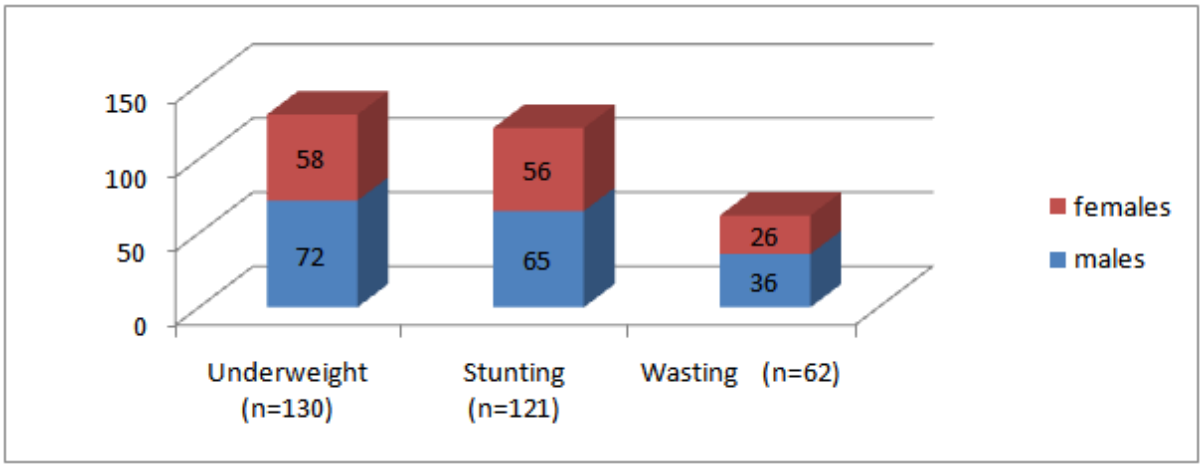

Fig 5: Prevalence of malnutrition in both sexes

Anthropometric indices	Total number of children n (%)	Girls n (%)	Boys n (%)	p-value
Study population	213	107	106	
WAZ<-2	130(61)	58(54.2)	72(67.9)	0.113
HAZ<-2	121(56.8)	56(52.3)	65(61.3)	0.347
WHZ<-2	62(29.2)	26(24.2)	36(33.9)	0.179

Table 3: Gender wise prevalence of malnutrition among HIV infected children

We examined the relationship between CD4% and the various growth parameters. We found that 34.27% (n=73) of the children were severely immunosupressed (CD4 %< 15%).Of these children with CD4<15%, 75.34% were underweight and 64.38% were stunted, 36.98% of children among these group were wasted.

In our cohort we have found that 90% of the underweight and wasted children have moderate to severe immunosuppression (CD4% <=25%). Around 85% of the stunted children were having moderate to severe immunosuppression.

Table 4. shows the prevalence of different types of malnutrition in children at different levels of immunodeficiency. Higher rates of moderate to severe stunting, underweight and wasting were observed among children with CD4 <15% compared to those at higher CD4%. There was a low or weak correlation between underweight and CD4% ($p<0.05$, $r=0.24$) and between wasting and CD4% ($p<0.05$, $r=0.13$).

Malnutrition scores	CD4<15% n=73(%)	CD4 15-25% n=103(%)	CD4 >25% n=37(%)
WAZ<-2*	55(75.34)	61(59.22)	14(37.83)
HAZ<-2	47(64.38)	57(55.33)	17(45.94)
WHZ<-2*	27(36.98)	29(28.15)	6(16.21)

* indicates p-value less than 0.05.

Table 4: Prevalence of underweight, stunting and wasting at different levels of immunodeficiency

IV. Discussion

In our study we included 213 children, 106(49.77%) were boys and 107(50.23%) were girls. Their age group was in the range of 4 to 60 months with a mean age of 36.32±18.93 months. In a study done by Michelle R Berger et al (2008) from Kenya, on a population group of 170 children, they observed 45.3% boys and 54.7% girls between the age group of 0 to 5 years (9). Our study also had almost same sex variability as with this study. Other studies included different age groups Padmapriyadarsini et al (2009) (10). Anita Shet et al (2009) (11).

The mean CD4 count in our study was 889.25±662.48 cells/cumm and mean CD4 % was 17.99±8.03.In a study done by Padmapriyadarsini et al (2009) the mean CD4 count was 793±614 cells/cumm and CD4 % was 17.7±10.2.In an other study Anita Seth et al (2009) has found the mean CD4 count as 582±401 cells/cumm in their population. Our study had almost similar CD4 counts and CD4 percentages as with the previous studies.

Our study has found that the prevalence of underweight was 61% (n=130). This is much higher than the national average of 48% underweight reported by NFHS-3 for under-five children (12). Our findings are similar to rates of undernutrition among HIV-infected children reported from other parts of India, which vary

from 60 to 62% (10,11,13,14). These figures are higher than those reported among HIV infected children in Africa (9,15,16).

In our study the prevalence of stunting was 56.8% (n=121) which is comparable to the values in studies done by Padmapriyadarsini et al (2009) (58%) and Anita Seth et al (2009) ie.46.37%.This is much higher than the national average of 40% stunting reported by NFHS-3 for under-five children (12).

In our study 29.2% (n=62) of the study population were found to be wasted comparable to Padmapriyadarsini et al (2009) with 16% and Anita Seth et al (2009) with 34.27%

Only 29.2% of children in our study were wasted indicating that proportion of growth failure is more likely in the setting of HIV infection rather than acute weight loss over a short period.

The pattern of growth failure among the children in our study suggested the prevalence of both relatively acute (underweight or low weight-for-age) and chronic growth failure (stunted or low height-for-age). The overall prevalence of wasting (low weight-for-height) was low, as seen in our study, suggesting that the majority of children with growth failure as indicated by underweight or stunting, were nevertheless, normally proportioned.

Our data highlights the much higher rate of moderate and severe grades of malnutrition among HIV-infected children in India. The children included in our study were seeking care at government health facilities and represent the majority of HIV-infected children in India, who are from socioeconomically vulnerable group.

Growth failure may be a direct consequence of the HIV infection, secondary to the clinical illness associated with HIV, a function of the child's adverse environment, or a combination of these factors. It is probable that, independent of HIV infection, malnutrition can reduce immunological function and can impair that child's ability to resolve acute infections. Low weight for age, like low haemoglobin, was an independent predictor of mortality among HIV-infected children in Zambia (17,18).

This is important as malnutrition has a major impact on the outcome of HIV disease as it not only increases mortality (15,16) but also results in an impaired response to antiretroviral therapy (19). Rajasekaran et al. showed that children who were severely malnourished at baseline, had a hazard ratio of 6.7 (0.9–49.4) for mortality after initiation of ART, compared to children who were normally nourished (20). However nutritional recovery and growth after treatment of malnutrition is similar to that observed in HIV uninfected children, stressing the need for early recognition and management (19). We explored this area in depth as only few studies from India have examined the pattern and type of malnutrition in detail or attempted to study its correlation with immune status.

In our study no immunosupression was seen in 34.27%(n=73), moderate immunosupression was seen in 48.35%(n=103) and severe immunosupression in 17.37%(n=37). In a study done by Padmapriyadarsini et al (2009) they found that 17%(n=33) had no immunosupression, 42.26%(n=82) had moderate immunosupression and 40.72%(n=79) had severe immunosupression. In a study done by Anita Seth et al they found that no immunosupression was found in 34%, moderate immunosupression was seen in 44% and severe immunosupression was seen in 22%.Our study had almost similar values compared to the above two studies done in South India.

In our study we have found statistically significant correlation ($p<0.05$) between underweight, wasting with immunosupression. In a study done by Padmapriyadarsini et al (2009) they had found a statistically significant correlation between underweight, stunting with immunosupression but not with wasting. In our study we did not get a statistical significant correlation of stunting and immunosupression.

In our study, the CD4 counts were lower in children with stunting and underweight compared to the age group as a whole—CD4% which are more stable than absolute counts also showed a decline. Wasting was relatively less prevalent in our cohort suggesting that malnutrition was of chronic onset and not an acute entity, unlike a report from Malawi where the commonest physical sign was wasting in more than 70% of the infected children (17).

Immune status and malnutrition showed a fair correlation in our study , 90% of cases with underweight and wasting had moderate to severe immunosupression (CD4 $\leq$ 25%) and about 85% of the children with stunting had moderate to severe immunosupression (CD4 $\leq$ 25%).

IV.1. Strength

The strengths of our study are that this was a group of well-characterized HIV-infected children representing below 5 years of age where there would be possibility of early prediction of malnutrition. Both anthropometric and CD4 measurements were performed using standardized methods.

Our study design precluded the comparison of growth abnormalities between HIV infected and noninfected children, as in comparison with non-infected children, HIV-infected children are likely to have increased nutritional requirements, poor appetite and reduced intake due to illness and socioeconomic factors [16].All these factors put a HIV infected child at risk of developing growth abnormalities.

IV.2. Limitations

Since this study was cross- sectional in design, it was difficult to examine any temporal relationships between malnutrition and disease outcomes. As very sick children (WHO clinical stage 4) were not enrolled in our study, there is a possibility of selection bias, thus under-estimating the actual prevalence of growth abnormalities. On the other hand, all these children came to a tertiary level centre to seek medical care and may therefore represent the more severely affected end of the spectrum.

IV.3. Recommendations

Nutritional supplementation can make a significant contribution to the care of children living with HIV by preventing or decelerating growth failure. To reduce the risk of HIV transmission, HIV positive mothers are advised to avoid breastfeeding and use replacement feeding.

Ms. Anuja Agarwala, Nutritionist, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi presented a paper on Special Nutritional Needs of Infected / Affected Children. She underlined that malnutrition in AIDS is multifactorial. In fact, HIV infected children will have several additional symptomless opportunistic infections and increased antibiotic resistance as well. She has suggested a guideline as the "nutritional goals" to be achieved according to Indian requirements (21,22)

As regards HIV infected children, they have increased calorific needs from early in the disease even before they become symptomatic. Early aggressive nutritional intervention even before the child becomes wasted with very low CD4 counts will reduce the risk of opportunistic infections, mortality and may delay HIV disease progression. Malnutrition in HIV/AIDS is reversible by tackling the quality of life and starting the feeding programs much before the child is in terminal state (23).

V. Conclusion

The high prevalence of underweight, stunting and wasting in the South Indian studies signifies the fact that targeted nutritional interventions need to be incorporated in the national programmes along with support and treatment among HIV infected children.

Our study reinforces findings that growth failure and malnutrition are major manifestations of HIV infection in Indian children with prognostic significance. In addition to continuing efforts in improving access to antiretroviral therapy, it is time to pay attention for further refining our therapeutic strategies by making nutritional counselling, nutrition supplementation and sustainable nutritional interventions as integral part of our overall approach in helping children with HIV live as normal a life as possible.

Key role of Nutrition and Health sector is well recognized. Nutrition indicators should be incorporated into HIV/AIDS monitoring and evaluation plans. Systemic operational and clinical research should be conductedto support evidence based interventions and strategies. Practical tools should be developed for nutritional assessment Control of AIDS calls for multi sectoral action –existing interventions should be expanded for improving nutrition. Strong Political support and political commitment are essential. It is necessary to develop and protect human capacity and skills for effective community participation.

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