Original Research :

Factors Influencing Adherence to Antiretroviral Therapy In Pediatric HIV

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Abstract:

Introduction: HIV infection has been recognized as pandemic by World health organization (WHO). Management of HIV includes a combination of antiretroviral drugs (ARV). It effectively suppress viral replication and improves quality of life if adherence is good. Maintenance of good adherence in children is difficult as they depend on their caregiver. So it is very important to assess the level of adherence and different factors influencing it. **Setting:** Pediatric ART centre of a tertiary care teaching hospital of West Bengal. **Study Design:** This was a prospective observational study. **Methods:** All children started on ARVs within first three months of study period with an identifiable caregiver were included in the study and followed up for next 9 months. Level of adherence was assessed by medicine return technique. Objective of the study was to assess the relationship between level of adherence to Antiretroviral therapy (ART) with different socio-economic, socio-demographic and therapy related factors and clinical, immunological staging of the disease. **Result:** 76.78% of the children were showing adherence to ART >=95%. Nutritional status of the child at the initiation of ART, socio-economic factors and disease severity were strongly related to level of adherence. Most common barrier of adherence was simple forgetting (35.71%). Conclusion: Level of adherence to ART should be assessed with every visit to the ART centre. Medicines return technique is quite good in this resource limited setting. By assessing the factors that can influence adherence we can identify the vulnerable population and we can give our extra attention to this group of children.

Introduction:

Global burden of HIV/AIDS disease was estimated to be 36.9 (34.3-41.4) million in 2014.[1] An estimated number of children living with HIV was 2.6 million in 2014. South East Asia is the second most affected region where 4.8 million people are living with HIV. It is 12% of all people with HIV [2]. In India, situation is much grimmer. In 2011, it is estimated that 20.9 lakh people are living with HIV and 7% of them are below 15 years of age1. Management of HIV includes multiple anti-retroviral drugs, which act on different viral stages in combination and it is known as highly active antiretroviral therapy (HAART). It is well established that success of HAART depends on its adherence. As defined by WHO, adherence is the degree to which the patient's behaviour is in agreement with the health care provider's recommendations. According to World Health Report 2003, the degree of medication non-adherence is so great and the consequences are of such concern that more people worldwide would benefit from efforts to improve medication adherence than from the development of new medical treatments. Non-adherence to ART is also very common. Average rate of non-adherence varies with method used to assess it. It has been shown that despite the critical need for strong adherence in HIV treatment many patients have difficulty in realizing this goal. Picture in children is not so optimistic. But it is proved that near perfect

(> 95%) adherence is necessary to achieve full and durable viral suppression[3,4]. In practice, this degree of adherence means not to miss more than 3 doses of antiretroviral medication per month in a twice-daily regimen. This degree of adherence is far more than that needed in case of other chronic diseases (Just 80%). Factors that can influence adherence in pediatric patients include social instability, unstable housing, and lack of disclosure, depression, family's perception of the disease and the value of its treatment, regimen complexity, pill burden, and tolerability[.5,6] Some of the factors are very important for pediatric patients like multiple medication, high pill burden, low palatability, large pills, significant short and long term adverse effects. (Nausea, rash, hypersensitivity, lipodystrophy, anemia). Family and caregiver factors are crucial to pediatric adherence, because they solely depend on caregiver for regular administration of drugs. Care-giver who are biological parents of HIV-positive children often share their diagnosis and confront challenges associated with their own disease burden. They are often too fatigued or debilitated physically and mentally to care their children. Good drug adherence is associated with improvement in CD4 count4 and mortality and morbidity[7]. But there are some controversies regarding non-adherence and drug resistance[8]. There are different methods to assess the level of adherence e.g. pill count, pharmacy refill record, electronic drug monitoring (EDM), resistance testing, therapeutic impact such as VL, CD4 lymphocyte count monitoring, caregiver report. The data from studies of pediatric ART adherence fail to provide definitive guidelines or to identify any gold standard in terms of assessment methods.

Objective:

To assess the relationship between level of adherence to ART with different socio-economic, socio-demographic and therapy related factors and clinical, immunological staging of the disease.

Methods:

This was a prospective observational study which includes 1 to 12 years old children who were started on ART during first 3 months of study period from Pediatric ART centre of a tertiary care teaching hospital of West Bengal with proper pre-ART counseling, having identifiable caregiver to administer medication, willing to comply with ongoing regular clinical attendance and monitoring. Socio economic and demographic factors (Age, sex, primary caregiver mother or not, his or her age and education and he or she employed or not, father provide financial support or not, they receive any social grant or not, housing, access to electricity and refrigerator) were assessed at the beginning of therapy from one to one interview with the caregiver. Current clinical and immunological staging was assessed from the available medical records. Weight and height was measured using standard methods. Level of adherence was measured by medicine return technique [MR] at the end of each month and whenever a significant non-adherence was reported, caregiver was interviewed for the cause of non-adherence. In medicine return technique, caregivers were requested to return all empty medicine containers and unused medications at every monthly visit for 9 months. The percentage adherence for each antiretroviral medication for each month was calculated by dividing actual use (Determined from returned containers and unused medication) by expected use (From the previous month's script). A composite measure of 9 months average percentage adherence by MR was calculated by determining the arithmetic mean. If mean adherence was below 95% it was considered significant non-adherence.

Categorical variables were expressed as Number of patients and percentage of patients and compared across the two groups using Pearson's Chi Square test for Independence of Attributes. Continuous variables were expressed as Mean ± Standard Deviation and compared across the two groups using unpaired t test. The statistical software SPSS version 16 has been used for the analysis. An alpha level of 5% has been taken, i.e. if any p value was less than 0.05 it was considered as significant.

Results:

Of the 57 children with confirmed diagnosis who were included in the study group and started ART in the first 3 months of study period and fulfilled the inclusion criteria, 76.78% of the children were showing adherence to ART >=95% and 23.22% were showing adherence <95% (significant non adherence). Among the study population42.9% was in WHO clinical stage 1, 12.5% in stage 2, 17.9% in stage 3 and 26.8% in stage 4. 26.8% of the study population were above 2SD line (No malnutrition) in WHO growth curve weight for age, 53.6% were between 2SD and 3SD line (MAM), 19.6% were below 3SD line (SAM). Among the children studied 57.1% had mothers as primary caregiver and 42.9 % had other person as care giver. 57.1%of the primary caregivers were below secondary education while 42.9% had. 85.7% of caregivers were unemployed and only 14.3% of care givers were employed. 85.7% subjects had formal housing while only 14.3% had informal housing (Footpath or slum dweller). In the study group, 16.1% patients did not have access to electricity while 83.9 % had the access. 78.6% did not have access to refrigerator while 21.4% had. Most common barrier of adherence in our study group was simple forgetfulness (35.71%). Other causes were sickness of the child, distance, medicine side effects, sickness of caregiver, residing away from home and apparent drug ineffectiveness.

Factors that can influence level of adherence were classified under some broad heading-demographic, socio-economic, disease related, nutritional, treatment related. Demographic factors like age, gender; religion had little impact on level of adherence. Nutritional status of the child at the initiation of ART (Weight for age, height for age) was strongly related towards level of adherence. Socio-economic factors like primary caregiver's relation with the child, his or her educational level, availability of father's financial support, formal housing, were all associated with good adherence. On the other hand, factors like caregiver employment status, availability of social grants and

access to refrigerator had no statistically significant relationship with the level of adherence. Factors determining diseases severity like good CD4 count, early WHO clinical staging were also significantly related to the level of good adherence.

Discussion:

In different studies, adherence levels have been measured by using different methods. The estimated adherence level also varies according to the method used. According to a review article[9] results of the studies those used caregiver reports, the mean adherence ranged from 88.4% to 96% while self-reported adherence ranged from 93% to 97%. High adherence level was estimated by two studies that used pill counts (Mean adherence ~87%)[10] though literature has shown that pill dumping and pill damage are two major drawbacks of this method.[11] In these cases, patients dispose some pill to make their adherence appear better than it may actually be. In our study, inadequate adherence was found in 23.22% of children. However, the level of adherence was fairly good in our study population in comparison to other studies.

The demographic factors in different studies were inconsistent. Some studies did not show any relation between drug adherence and race, gender[12] but some have suggested that older children are more likely to be non-adherent. In our study we did not find any demographic factor to be significant.

The WHO clinical stages are found to be associated with severity ofdisease, opportunistic infections and increased number of daily medications. There are a few studies that describe a relationship between disease severity and non-adherence[13,14] but against this opinion there are two studies which showed increased adherence in those having a opportunistic infections[15,16.] It is postulated that their experience with bad health ignited their desire for good health and thus motivated for adherence. On contrary it is also true that severity of the disease associated with increased pill burden which is associated with bad adherence.[17] We find

that an association between increasing WHO clinical staging and non-adherence and it is mostly due to increased number of opportunistic infections, increased number of daily medications and increased rate of hospitalization.

Malnutrition and HIV may interact in a vicious cycle, where malnutrition accelerates immune-suppresion and HIV infection worsens malnutrition.[18] Poor nutrition may also affect a patient's adherence to antiretroviral therapy (ART) by depriving him or her of the energy to travel to the pharmacy to collect antiretroviral drugs[19] or by potentiating drug toxicity[20].In the present study it was found that low weight for age and low height for age Z scores are associated with non-adherence.

Family/caregiver factors are crucial to pediatric adherence, because infants and younger children depend almost entirely on a caregiver to administer medications. Mother is always the best caregiver because mothers and children are biologically related and dependent. So it is evident that when mother is present and enough healthy to take care of her child, adherence to ART will be good. In our study it was also found that good adherence was associated with children who were cared by mother. But some studies showed caregivers who were biological parents of HIV-positive children often shared their diagnosis and confronted challenges associated with their own illness, besides its co-morbidities. Thus, they may be physically fatigued or debilitated. In these cases, treatment may became a reminder of parents' guilt about their role in their child's acquisition of

infection, which was yet another challenge to adherence.[21] A study conducted in the Cape town had shown that socio-economic status was strongly associated with better adherence.[22]

In a 2006 meta-analysis of 18 studies of adherence to HAART, which included both children and adults, simply forgetting to take medications was most commonly reported as a barrier (37%).[23] In our study we also found that simple forgetting was the most common barrier, followed by distance and side effects.

There are some limitations in our study like medicine return was used as sole method to assess adherence. Psychological factors like depression are important but not assessed in our study. Nine months follow up could be a shorter period as ART supposed to be life-long.

So assessment of the adherence level is an important part of antiretroviral therapy. Level of adherence to ART should be assessed with every visit to the ART centre. Medicine return technique is quite good in this resource limited setting. By assessing the factors that can influence adherence we can identify the vulnerable population and we put our extra attention to this group of children to ensure good adherence. Some factors can be modified like ensuring good nutrition with help of ICDS or mid-day meal programme. Above all good psycho-social support can re-establish the broken dreams and can provide a new ray of hope that HIV is not the end; a good adherence to ART can give them a healthy tomorrow.

What is Already Known	1. Near perfect (> 95%) adherence is necessary to achieve full and durable viral suppression 2. Different socioeconomic, sociodemographic, treatment related factors influence level of adherence
What this Study Adds	1. Factors associated with caregiver deeply influence level of adherence in pediatric patients. 2. Nutrition is an important factor that influence level of adherence 3. Simple forgetting is the most common barrier followed by distance and side effects.

RCS- Reviewed Literarture And carried out clinical work , SA –Helped RCS In TECHNICAL AND CLINICAL WORK , DAK - Concept And Guidance, DK-Statistics And Analysis, DS-Critical Review Of Article

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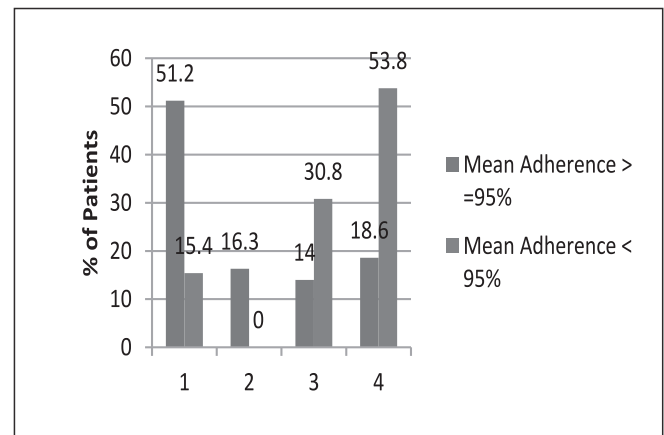
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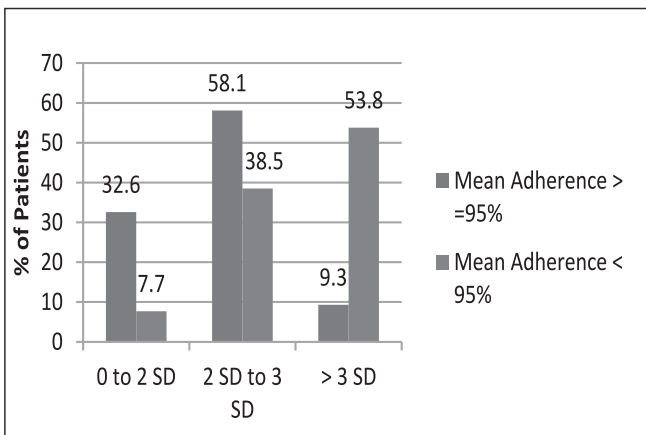
Fig. 1. Relationship between weight for age z score and level of adherence.

Fig. 2. Relationship between WHO Clinical Staging and Adherance to ART in Study Group

Table1: Relationship between education of caregiver with child and level of adherence

	Mean Adherence				
CAREGIVER EDUCATED	> =95%	< 95%	Total	P Value	Significance
NO	19(44.2)	13(100)	32(57.1)	<0.001	Significant
YES	24(55.8)	0(0)	24(42.9)		
Total	43(100)	13(100)	56(100)		

Table 2: Showing different barriers of adherence

CAUSE OF NON ADHERENCE	
FORGETFULNESS	5(35.71%)
SICKNESS OF THE CHILD	2(14.28%)
DISTANCE	1(7.14%)
SIDE EFFECT OF THE DRUGS	2(14.28%)
AWAY FROM HOME	1(7.14%)
APPARENT INEFFECTIVENESS OF THE DRUG	2(14.28%)