

Association between Paediatric ART Clinic Attendance and Treatment Failure in HIV Infected Children Attending a Nigerian Hospital

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Abstract— Background: Regular anti-retrovirals clinic attendance is necessary for re-fills of consumed HAART as this will affect adherence. The association between the regularity of clinic appointment attendance, adherence and treatment failure (TF) in Nigerian children is unknown. Other factors influencing associated with TF also need to be studied. **Objective:** To determine the association between clinic attendance and treatment failure and other factors associated with treatment failure. **Method:** Consecutive consenting HIV infected children and their care attending the Paediatric ART clinic of a Nigerian hospital were studied. Information on the socio-demographics of the caregiver and the HIV infected children were obtained. Additional details sought and recorded in a proforma include clinic attendance over a two year period and the latest CD4 and viral load count over this period. Data obtained was inputted into a personal computer and analysed using SPSS version 16. **Results:** The ages of the 30 children studied, ranged from 3 months to 11years, with a mean of 5.6 ± 2.4 . Of these children, 15(50.0%) were boys and 15(50.0%) girls giving a male to female ratio of 1: 1. Eight (26.7%) of the 30 children had an attendance rate > 95% in the two years period of study and the remaining 22(73.3%) attended less than 95% of the expected times. Persistent virological and immunological treatment failures with viral loads >1000copies/ml and CD4counts < 200cells/ul were recorded in 13(43.3%) cases and 1(3.3%) case each respectively. Six (20.0%) children were from the upper social class, 9(30.0%) from the middle class and 15(50.0%) from the lower social class. The 8 children with attendance rates above 95% had significantly reduced rates of treatment failure, while the greater number of children from the lower social classes had significantly greater rates of treatment failure compared to those in the upper and middle social classes. ($p < 0.05$). **Conclusion:** The majority of the children studied had less than 95% attendance rate. Virological treatment failure is not uncommon among the studied subjects. The significant association between paediatric ART clinic attendance rate <95% of expected times and virological treatment failure makes it imperative to discover strategies that will encourage optimal clinic attendance.

Keywords— Adherence, resistance, HIV infection, Childhood.

I. INTRODUCTION

Treatment failure is a common problem associated with HIV infected children in developing countries^{1,2,3} Poor adherence to highly active anti-retroviral therapy is the most common and important reason responsible for the development of treatment failure. A previous study showed that the care givers socioeconomic status, the gender of the child, having a medication reminder strategy, HIV disclosure status and the regularity of paediatric ART clinic visits were some of the factors determining adherence to HAART.⁴

Timeliness of clinic has been shown to be a good predictor of virological response and resistance to anti-retroviral drugs in HIV infected patients.⁵ Evidence indicates that a 95% adherence rate is key for prevention of treatment failure.^{6,7} Regularity of clinic attendance is thus vital, as the ART clinic is the source of obtaining necessary medications and re-fills as at when due. In addition, regular clinic attendance also gives the opportunity to adjust and revise doses of medications in the growing children. Regular revision of drug doses in the growing child is as important as refills, because suboptimal dosages of HAART medications have been found to lead to drug resistance and treatment failure.

II. METHODOLOGY

Information on the socio-demographics and the clinic attendance of consecutive children attending the Paediatric ARV clinic between 2013 and 2016 were studied. The attendance of the children over a two year consecutive period was obtained from the HAART record unit. The HIV status of the parents was also sought. In addition, details of the most recent viral load and CD4 counts of the children were obtained from the case notes of the studied children. All the information obtained were recorded in a proforma.

The occupations and educational attainments of both parents were obtained. The socioeconomic classification of the parents was computed, based on the occupation and educational status of the parents as classified by Oyedeji et al.⁸ Social classes of the children were determined by allotting scores for the different occupations and educational attainments which were summed up and the mean of the final score was equivalent to the different social classes. Social classes I and II were further sub-classified to give the upper social class and social class three the middle and social class IV and V the lower social class, based on Oyedejis socioeconomic classification.⁸

The staging of HIV in the infected children was based on the WHO, clinical staging.⁷ Attendance of the children was classified as attendance rates above and less than 95% of the

12 visits expected over a two year period, considering that statutory clinic appointment frequency is once every two months. A 95% attendance rate was set as the cut off, because attainment of this rate should ensure availability of HAART medications to meet a 95% adherence rate, which is the standard needed to prevent resistance or treatment failure.⁸

All information obtained was imputed into a personal computer and analyzed using SPSS version 16.¹⁰ Categorical data was expressed as percentages, while numerical data was expressed as means and ranges, P values less than 0.05 were accepted to be significant.

III. RESULTS

General characteristics

A total of 30 children and their caregivers were studied. The care giver accompanying the children to the clinic was the mother in 26(86.7%), father in 3(10.0%) and step mother in a case.

Age and sex distribution of children studied

The ages of the children studied ranged from 3 months to 11years. The mean age of the children studied was 5.6 ± 2.4 . Twelve (40.0%) of the 30 children were aged between 3months and 5years, while 17(56.7%) aged between 6 – 10years and 1(3.3%) aged between 11 – 15years. Of the 30 children studied 15(50.0%) were boys and 15(50.0%) girls giving a male to female ratio of 1: 1. The age and sex distribution of the children studied is shown in Table I.

TABLE I. Age and sex distribution of the children studied

Age	Gender	
	Male	Female
Age group		
3months – 5 years	6	6
> 5 years – 10years	9	8
> 10 years – 15 years	0	1
Total	15	15

Age distribution of the parents

The ages of the fathers ranged from 30 – 71years with a mean of 43.7 ± 1.0 years, while the range was 22 – 54 years with a mean of 35.7 ± 6.6 years for the mothers.

Clinic attendance of the children studied

Of the 30 children studied, over the 2 year period, 8(%) attended clinic the 12(100.0%) maximum times the clinic held, while 11 children attended 11(92.0%) times. The number and proportions of paediatric ART clinic appointment kept by the children are shown in Table II.

Clinic attendance and computed adherence

Based on the regularity of attendance, only the 8 children who attended 12 times achieved an attendance rate of 100%, which was the only rate which could give the envisioned adherence rate $\geq 95\%$, if both caregivers and the HIV infected child observe the practice of taking the HAART medications as prescribed and obtained at the Paediatric ARV clinic. This is the minimum expected adherence rate projected for optimal therapeutic effect of HAART.

TABLE II. Clinic attendance of the children over the two 2year study period

Number (%) of children (N = 32)	Number of clinic visits (Maximum no of clinic visits n =12)	Percentage of the total maximum visits (expected maximum visits =12)
1	6	50.0
1	7	58.3
1	8	67.0
1	9	75.0
7	10	83.0
11	11	92.0
8	12	100.0

Treatment failure

Of the 30 children studied 13(43.3%) had virological treatment failure with persistent viral load >1000 copies/ml and 17(56.7%) had normal viral load suppression with viral load < 1000 copies/ml Immunological treatment failure was recorded in 1(3.3%) patient with CD4 count <200 cells/ul, while 29(95.7%) were immune competent with CD4 count > 200 cells/ul.

Association between age and sex distribution and treatment failure

Seven(63.6%) of the 11 children aged between 3months to 5 years had virological failure, while the only child aged older than 10 years did not experience treatment failure. The association between treatment failure and the age group is shown in Table III. Seven (46.7%) of the 15 boys had virological treatment failure while 6(40.0%) of the 15 girls experienced virological treatment failure. The association between gender and treatment failure is shown in Table III.

WHO clinical staging of the children studied

Of the 30 children studied 2(6.7%) children had stage I disease, while 12(40.0%) had stage II disease and 16(53.3%) had stage III disease. None of the patients studied had stage IV disease or AIDS. The association between WHO clinical staging and virological treatment failure is shown in Table III.

Residential location of the children and caregivers studied

Most of the children resided in locations less than 100km from the health facility, with 23(76.7%) living in homes situated less than 100 kilometres from the health facility, while 7(23.3%) lived in homes located beyond 100km from the health facility. Thirteen (43.3%) of the HIV infected children and their care givers resided in the Osogbo town where the health facility was situated. Of the 30 children studied 4(13.3%) lived in locations that were remote, and rural, where it was difficult to access the health facility from the patient and caregivers home setting. The association between the locations of the HIV infected children and treatment failure is shown in Table III.

Parental educational attainments

Concerning educational training amongst the fathers, 4 (13.3%) had university education, 7(23.3%) had a higher national diploma equivalent, while 5(16.7%) had secondary, modern and technical school equivalent education, 13(43.3%) primary school and 1(3.3%) father had no formal education. Concerning the mothers 2(6.7%) had university education,

while 7(23.3%) had higher national diploma and equivalent education, 9(30.0%) had secondary, modern and technical school equivalent education, 10(33.3%) had primary school and equivalent education. The remaining 3(6.7%) mothers had no formal education.

TABLE III. Association between adherence and age group, gender, HIV clinical staging and social class

	Virological failure		P value	X ²
	Yes	No		
Age groups				
3mths – 5 years	7	4	2.31	0.31
6 – 10 years	6	11		
11 – 15 years	0	1		
Gender				
Male	7	8	0.14	0.71
Female	6	9		
Clinic attendance				
Attendance > 95% expected	1	7	4.2	0.04
Attendance < 95% expected	12	10		
WHO HIV Clinical stage				
I	1	1	0.81	0.67
II	4	8		
III	8	8		
Social class				
Upper	0	5	6.58	0.04
Middle	3	6		
Lower	10	6		
HIV Status of parents				
Discordant	8	6	2.29	0.32
Same status	2	6		
Can't be classified	3	5		
Orphans				
Yes	3	5	0.15	0.70
No	10	12		
Relation between residence of patient and health facility				
< 100km	11	12	0.81	0.37
> 100km	2	5		
Relation between residence setting and health facility				
Easily accessible	10	14	0.14	0.71
Remote	3	3		

Occupational categories of parents

Concerning the vocation of the fathers, 7 (23.3%) were in the highly skilled professional groups such as accountants, engineers, lawyers, doctors and big time entrepreneurs, 1(3.3%) father was a lecturer at the polytechnic, while 4(13.3%) were in the cadre of police officers, secondary school teachers and middle grade trader and the remaining 18(60.0%) were artisans such as mechanics, panel beaters, carpenters and tailors. Concerning the mothers 3(10.0%) were in the grade of administrators and accountants, while 7(23.3%) were in the grade that were lecturers at polytechnics, school of nursing and technical schools and the remaining 18(60.0%) were artisans, such as hairdressers, tailors and middle grade traders.

Social classes of the children studied

Of the 30 children studied 4(13.3%) were from social Class I, 2(6.7%) from social class II, 9(30.0%) from social class III, 14(46.7%) from Social Class IV and 1(3.3%) from

social class V. Thus 6(20.0%) children were from the upper social class, 9(30.0%) from the middle class and 15(50.0%) from the lower social class. The association between virological treatment failure and social class of the studied children is shown in Table III.

Status of the parents with respect to life

Of the 30 fathers studied 25(83.3%) were alive at the time of study, while 26(86.7%) of the mothers were alive. Thus 8 of the children were orphans, with one of the children haven lost both dad and mum. The association between status of the parents whether alive and dead and virological treatment failure is shown in Table III.

HIV status of the parents

Fourteen fathers (46.7%) were HIV negative, while 8(26.7%) had HIV positive status and 8(26.7%) fathers did not know their HIV status. Of the 30 mothers 28(93.3%) were HIV positive and 2 (6.7%) were HIV negative. Of the total parents studied 8(26.7%) parents had the same HIV status, while 14(46.7%) parents had a sero-discordant status, while 8(26.7%) parents could not be classified because either the dad or mum did not know their HIV status. The association between the HIV status and virological treatment failure is shown in Table III.

IV. DISCUSSION

The present study showed a significant association between clinic attendance and treatment failure. This is an expected finding. The importance of timeliness in the attendance of Paediatric ART clinics as a predictor of treatment outcome has already been highlighted.⁵ Timeliness of clinic attendance is however based on an assumption that the regularity of clinic attendance correlates with adherence with HAART. A study conducted in HIV infected adults in Uganda recorded a statistically significant association between regular clinic attendance and adherence to HAART.⁹ Previous studies also confirm that a good adherence to HAART medication is a necessary pre-requisite in order to avoid treatment failure.^{2,11,12}

In the present study there was no gender predilection of subjects as we had both equal number of boys and girls. A previous study reported a significant association with adherence among the male sex.⁶ Furthermore, similarities in the age group studied in the present study and those of other report also exist, however the significance of association of age or gender of the HIV infected child or care giver with clinic attendance was not tested. Ugwu et al, however documented age less than 5 years and missed clinic visits as common reasons for poor adherence, the gender of the child had no significance with adherence.⁴ The variations in the selection of the study participants in the available studies make comparison of the results of this study a challenge with previous studies.

In the present study, less than a third of the children studied achieved an adherence rate above 95%. This result is alarming and may explain the unacceptably high rates of virological treatment failure recorded. A plausible explanation

for our finding is that the poor clinic attendance translated to poor adherence, thus leading to the high rates of virological treatment failure recorded.

Significantly higher rates of virologic treatment failure were recorded among the lower socioeconomic classes in the present study and all the children in the upper socioeconomic classes did not experience treatment failure. This finding may have to do with better access and utilization of health services known to be associated with the upper socioeconomic classes. Reports from previous studies are also consistent with our present findings; however the findings from the previous reports recorded no significance of association.^{4, 12}

Quite surprisingly, residential location of the patient, in terms of nearness or ease of accessibility to the health facility did not seem to have any negative or significant association on virologic failure. Unfortunately, the association between regularity of clinic attendance and nearness or accessibility to the health facility was not tested in the present study. The benefit of testing this association may be doubtful, so long as the end point of adherence and good clinical response to HAART is achieved. It is noteworthy that other factors such as stigmatization and individual preference may serve as confounding determinants of choice of health facility to access care and not the nearness or ease of accessibility.^{13,14}

Been an orphan also did not have any significant association with the development of virologic treatment failure in the present study. Possible explanation for this finding may have to do with other factors such as the attitude of the guardian or the HIV infected children, especially, if they are old enough to adhere to their HAART prescriptions by themselves. Other factors that may help with adherence to HAART and prevent resistance in orphans may include use of reminders such as phones, alarms and peer groups. It is also needful to state that there was only one complete orphan in the present study who had lost both parents and it is quite possible that the single orphans had a parent, that was up to the task of ensuring adherence. Our result in the present study are consistent with Iroha et al, however Mugusi et al,¹⁵ reported a poor adherence in orphans as a result of financial constraints and low knowledge of HIV infection on the part of the caregivers.^{12,15}

It is concluded that virologic treatment failure is common among this group of HIV infected children studied. Regularity in Paediatric ART clinic attendance is germane to prevention of virologic treatment failure. Interventions and strategies that will improve Paediatric ART clinic attendance need to be put in place by the government and the health care providers, in order to control the burden of treatment failure.

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