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Clinical Characteristics of Children with HIV Initiated on Antiretroviral Treatment at HIV Clinics in Bloemfontein, South Africa

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ABSTRACT

Background and Objective: Over the past 15 years, there have been three major updates to the South African national guidelines for the management of human immunodeficiency virus (HIV) in children. The purpose of this study is to describe the clinical characteristics of children who were initiated on antiretroviral therapy (ART) in Bloemfontein, South Africa, following these national treatment guidelines.

Methods: Clinical information during initiation of ART in children aged 0-13 years was obtained from five HIV clinics in Bloemfontein from 2004 to 2019 as part of the establishment of an antiretroviral (ARV) pediatric registry at the University of the Free State. Data were analyzed for patient demographics, clinical presentation (World Health Organization (WHO) HIV-staging, growth rate and comorbid conditions), types of investigations done, and medicines prescribed.

Results: The number of children initiated on ART increased from 168 in the period 2004-2009 to 349 (107.8%) in 2010-2014, and then dropped to 162 in the period 2015-2019. The increase in 2010-2014 was mainly in the <2 years age group by 54.8%, and in the 5 to 10 years age group by 344.4%. In the same period, the number of children with severe illness (WHO HIV-stage 4) decreased by 20.7%, while those with mild to moderate illness (WHO HIV-stage 2 and 3) increased by 17.3%. HIV infection was more severe in children under two years as more patients in this age group presented with WHO HIV-stages 3 and 4, severe underweight (below 3rd percentile), severely suppressed CD4 count (< 25%), and a high viral load (> 1000 copies/ml). There was increased use of ABC/3TC/LPVr in the < 3-year age group and ABC/3TC/EFV in the > 3-year age group. There was reduced use of the stavudine and other regimens.

Conclusion and Global Health Implications: More children were started on ART and safer ARV drugs. Children under 2 years were the most debilitated by HIV, and there was an increase in HIV prevalence among children > 5 years. New strategies for the prevention and management of HIV among children in these two age groups are needed.

Keywords: • HIV Infection • Children • ART Initiation • ARV Therapy • ARV-Guidelines • ARV-Pediatric Registry • South Africa • Child Health • HIV • Pediatric HIV • Treatment Guidelines

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1. Introduction

1.1. Background of the Study

Antiretroviral therapy (ART) has improved the care and survival of children with the human immunodeficiency virus (HIV) to the extent that ART is now recommended for initiation in children immediately after an HIV diagnosis.[1-4] In South Africa, the national antiretroviral (ARV) treatment guidelines for the care of children with HIV have been circulated to all relevant clinics to ensure consistent, standardized, and effective care for children with HIV. However, implementation of the national ARV treatment guidelines in children is complicated by growth-related changes in children's physiology and immunopathology to HIV, which cause children to require different treatment by age, weight, comorbid conditions, and the choice and formulation of drugs, among other things.[5] Implementation of the ARV treatment guidelines is also constrained by the lack of skilled healthcare personnel and inadequate infrastructure for the provision of health services. All these factors limit children's access to healthcare, thereby delaying early detection and treatment of HIV.[6]

The successful implementation of the treatment guidelines for the care of pediatric HIV patients requires continuous monitoring and adjustments regarding changes in patient or disease characteristics and/or the introduction of new treatment modalities.[6] Because such constraints affect different communities in different countries differently, there have been calls for evidence-based guidelines for the care of pediatric patients with HIV to be adapted to the capacity of the respective community health facilities.[7-8] This adaptation will enable healthcare providers to understand and address specific community needs and/or problems that hinder the successful implementation of the prescribed treatment guidelines. Unfortunately, despite the several updates in the South African HIV treatment guidelines, there is no information on the impact of these changes on the status of children with HIV and by which to improve the local practice guidelines.

1.2. Objectives of the Study

The purpose of this study is to examine the impact of national HIV treatment policy changes on the initiation of ARV treatment in children with HIV at five HIV clinics in Bloemfontein, South Africa. Specifically, this study describes the characteristics of children with HIV infection during the initiation of ART in the Bloemfontein ARV-clinics over a 15-year period.

2. Methods

2.1. Study Design

This study was the initial phase in establishing an ARV-pediatric registry at the Department of Pharmacology, University of the Free State, South Africa. It is a retrospective analysis of clinical information of children 0-13 years who were newly diagnosed with HIV and their subsequent management from initiation of ART at five HIV clinics in Bloemfontein over 15 years (2004 – 2019). The information collection point was the HIV clinic where the child attended for HIV care, and therefore had his/her clinical records. Data were collected from the clinics by trained technical personnel (nurses and pharmacy assistants) using questionnaires according to standard operating procedures. The study data were then transferred to an electronic questionnaire in the Research Electronic Data Capture (REDCap) software (Redcap Project, http://project-redcap.org) hosted at the University of the Free State.[9, 10] Double data-entry method was used to ensure accurate electronic data capture. At the time of the study, all patients in the registry were from the five ARV-clinics in the Bloemfontein metro: (1) Free State HIV-Clinic A (FSA), (2) Free State HIV-Clinic B (FSB), (3) Free State HIV-Clinic C (FSC), (4) Free State HIV-Clinic D (FSD), and (5) Free State HIV-Clinic E (FSE).

2.2. Study Variables

The information sought included the patient's demographics (gender, weight, age, etc.), clinical presentation and HIV diagnosis (signs and symptoms, WHO-staging, comorbidity, etc.), investigations have done (laboratory and other), ARV-drugs initiated and other drugs prescribed.

2.3. Statistical Analysis

The information was evaluated for three time periods: (1) 2004-2009; (2) 2010-2015; and (3) 2015-

2019, each corresponding to the implementation of the respective National HIV treatment guidelines. Age was categorized into < 1 year, 1 to less than 2 years, 2 to less than 3 years, 3 to less than 4 years, 4 to less than 5 years, 5 to less than 10 years, and 10 to 13 years. CD4 count was categorized into severe (<15%), moderate (15-24 %) and mild (≥ 25%). ART regiment was categorized into ABC/3TC/ LPVr, ABC/3TC/EFV, 4dT/3TC/EFV and other. Data analysis was done using Stata IC statistical software, version 16 (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC.), and was reported in frequency tables and distribution of the categorized variables. Growth data were assessed by percentiles derived from plotting the children's weights against their age using the WHO sex-appropriate growth standards.[11]

2.4. Ethical Approval

The study was approved independently by each of the following authorities: the University of the Free State Human Ethics Committee (UFS-HSD2018/0454/3107), the Free State Department of Health, the respective District Health Officers and the Chief Executive Officers of each of the five ARV-clinics. The electronic data was rid of personally identifiable information.

3. RESULTS

3.1. Demographic Characteristics

Table 1 (part 1A) shows the distribution of patients among the five HIV clinics. In total, there were 679 patients, comprising of 347 males and 322 females. Each of the five clinics experienced an increasing number of patients in the policy period of 2010 to 2014. The total number of children initiated on ART in this policy period increased from 168 to 349 (107.8%) (Figure 1a). There was an increase in the number of children less than 2 years (54.8%) and those in the 5-<10 years (344.4%) age groups. The number of children initiated on ARV dropped from 349 to 162 patients for the policy period 2015-2019.

Table 1 (part 1B) shows that children in the <2 years age group and those in the 5 to < 10-year age group were the most infected by the disease. Together, the two age groups accounted for 59.5%,

Table 1: The number and proportion (%) of patients (Pts.) that were initiated on antiretroviral therapy (ART) during each policy period; per clinic (Part 1A), by age group (Part 1B) and with comorbid conditions (Part 1C)

Period	2004-2009		2010-2014		2015-2019		
	Pts.	(%)	Pts.	(%)	Pts.	(%)	Total
Part 1A: Patients seen at the 5 clinics							
Clinic FSA	15	8.9	79	22.6	41	25.3	135
Clinic FSB	64	38	63	18.1	4	2.5	131
Clinic FSC	21	13	60	17.2	36	22.2	117
Clinic FSD	47	28	63	18.1	34	21.0	144
Clinic FSE	21	13	84	24.1	47	29.0	152
Total	168	100	349	100	162	100	679
% of total	24.7		51.4		23.9		
Male	81	48.2	183	52.4	83	51.2	347
Female	87	51.8	166	47.6	79	48.8	332
Part 1B: Patients initiated on of ART by age group							
	Pts.	(%)	Pts.	(%)	Pts.	(%)	Total
< 1 Year	35	20.8	68.0	19.5	32	19.9	135
1- < 2 Years	38	22.6	45.0	12.9	26	16.1	109
2- < 3 Years	26	15.5	28.0	8.0	15	9.3	69
3- < 4 Years	20	11.9	29.0	8.3	8	5.0	57
4- < 5 Years	22	13.1	39.0	11.2	7	4.3	68
5 - < 10 Years	27	16.1	120	34.4	50	31.1	197
10 - 13 Years	0.0	0.0	20	5.7	23	14.3	43
Total	168	100	349	100	161	100	678
Part 1C: Patients with comorbid conditions							
	Pts.	(%)	Pts.	(%)	Pts.	Pts.	Total
Tuberculosis	43	25.6	61	17.5	23	14.2	127
Pneumonia	15	8.9	27	7.7	12	7.4	54
Malnutrition	6	3.6	12	3.4	6	3.7	24
Other	13	17.7	34	9.7	33	20.4	80
None	91	54.2	215	61.6	88	54.3	394
Total	168		349		162		679

66.8% and 67.1%, of children initiated on ART in the three policy periods, respectively (Table 1, part 1B). Moreover, the proportion of children < 2 years of age who were initiated on ART remained high (over 30%) in each of the policy periods: 43.4%, 32.4% and 36%, respectively. The most worrying was the increase in the proportion of children 5 to <10-year age, from 16.1% in policy period 2004-2009, to 34.4%
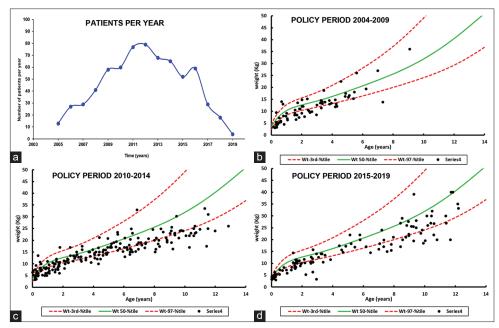
Figure 1: Plots for number of patients initiated on ART per year (a), and growth charts for HIV Children 0 - 13 years correlated with the normal growth percentiles for policy period 2004-2009 (b), 2010-2014 (c) and 2015-2019 (d)

and 31.1% in policy periods 2010-2014 and 2015-2019, respectively. The increase was also observed in children of the 10-13 years age group, from 5.7% in the period 2010-2014 to 14.3% in 2015-2019.

3.2. Clinical Presentation and Diagnosis

Growth: Figure 1b-d shows the weight versus age growth chart for the children. Whereas the growth of most children older than 2 years was in the 3rd percentile and above, that for the majority of children under 2 years was below the 3rd percentile, meaning they were severely underweight.[11]

WHO HIV-staging: Table 2 summarizes the WHO HIV stages per age group. The proportion of patients who presented with severe HIV (WHO HIV-stage 4) at the initiation of ART in the policy period 2010-2014 dropped by 21.5%, compared to the proportion in the 2004-2009 policy period, while the combined proportions of patients presenting with mild to moderate HIV (WHO HIV-stages 2 and 3) increased by 16.9%, and that for patients with WHO HIV-stage 1 increased by 4.5%. The changes in the policy period 2015-2019 mirrored that of

the policy period 2010-2014. The drop in patients presenting with severe HIV was partly due to similar improvements in the clinical presentation by children < 2 years of age where the proportion with WHO HIV-stage 4 dropped to 5.7% in 2010-2014 from 18.8% of 2004-2009. The increase in patients who presented with mild-moderate HIV was associated with an increase in the number of children of 5 - < 10 years who presented with WHO HIV-stages 2 and 3, from 10.4% in 2004-2009 to 28.2% in 2010-2014.

Comorbid conditions: Several comorbid conditions were identified. With the exception of tuberculosis, malnutrition and pneumonia, each of the comorbidities had a prevalence of < 1.5%. Table 1 (part 1C) shows the number of patients with concomitant tuberculosis, malnutrition and pneumonia during the three policy periods, 2004-2009, 2010-2014 and 2015-2019, and confirms that tuberculosis was the common comorbid condition. When data was evaluated by age groups, children in the < 3 years age group and those in the 5 to < 10 years age group accounted for the majority of

Table 2: The number and proportion (%) of patients (Pts.) by each age-group for each WHO-stage at the initiation of antiretroviral therapy (ART) in each policy period

	WHO stage_1		WHO stage_2		WHO stage_3		WHO stage_4		Total	
	Pts.	(%)	Pts.	(%)	Pts.	(%)	Pts.	(%)	Pts.	(%)
Period 2004-2009										
< 1 Year	1	1.0	6	6.3	7	7.3	12	12.5	26	27.1
1- < 2 Years	1	1.0	4	4.2	8	8.3	6	6.3	19	19.8
2- < 3 Years	1	1.0	2	2.1	10	10.4	3	3.1	16	16.7
3- < 4 Years	2	2.1	2	2.1	3	3.1	3	3.1	10	10.4
4- < 5 Years	0	0.0	2	2.1	6	6.3	2	2.1	10	10.4
5 - < 10 Years	0	0.0	2	2.1	8	8.3	5	5.2	15	15.6
10 - 13 Years	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Total & %age	5	5.2	18	18.8	42	43.8	31	32.3	96	100.0
Period 2010-2014										
< 1 Year	2	1.0	5	2.6	20	10.3	7	3.6	34	17.4
1- < 2 Years	0	0.0	2	1.0	20	10.3	4	2.1	26	13.3
2- < 3 Years	2	1.0	2	1.0	9	4.6	2	1.0	15	7.7
3- < 4 Years	2	1.0	6	3.1	10	5.1	1	0.5	19	9.7
4- < 5 Years	3	1.5	8	4.1	9	4.6	4	2.1	24	12.3
5 - < 10 Years	9	4.6	22	11.3	33	16.9	2	1.0	66	33.8
10 - 13 Years	1	0.5	3	1.5	6	3.1	1	0.5	11	5.6
Total & %age	19	9.7	48	24.6	107	54.9	21	10.8	195	100.0
Period 2010-2014										
< 1 Year	1	1.1	0	0.0	10	10.5	5	5.3	16	16.8
1- < 2 Years	0	0.0	1	1.1	14	14.7	2	2.1	17	17.9
2- < 3 Years	0	0.0	3	3.2	4	4.2	2	2.1	9	9.5
3- < 4 Years	0	0.0	1	1.1	4	4.2	0	0.0	5	5.3
4- < 5 Years	0	0.0	2	2.1	2	2.1	0	0.0	4	4.2
5 - < 10 Years	5	5.3	9	9.5	11	11.6	2	2.1	27	28.4
10 - 13 Years	0	0.0	9	9.5	5	5.3	3	3.2	17	17.9
Total & %age	6	6.3	25	26.3	50	52.6	14	14.7	95	100.0

patients with tuberculosis (Table 4). The proportion of children in the < 3 years age group with tuberculosis was 60.6%, 34.4% and 52.1% in the three policy periods, respectively, while the proportion for those in the 5 to < 10 years age group increased from 14.0% to 41% and 30.4%, respectively.

Pneumonia was predominantly found in children < 3 years (86.7%) during the policy period 2004-2009 (Table 4). Although lower, the prevalence of pneumonia remained high in children < 3 years (66.6% and 58.3%), but it also increased in those

5 - < 10 years, i.e., from 6.7% in 2004-2009 to 18.5% and 25% in the policy periods 2010-2014 and 2015-2019, respectively.

CD4 Counts and Viral Load: Table 3 (Part 3A) shows the effect of the disease on the CD4 count in each age group. Changes in CD4 count over the three policy periods depicted an improvement in the severity of the HIV. Whereas during the 2004-2009 policy period, a high number (49.2%) of patients presented with severely suppressed CD4 counts (<200 cells/ul or < 15%) and the majority

Table 3: The number of patients by age group and CD4 count (Part 3A) who were initiated on the different ARV regimens (Part 3B) in each policy period.

Part 3A	Reduction in CD4 count				Part 3B	ARV-regimens initiated				
	Period: 2004-2009:					Period: 2004-2009:				
CD4 grade	Severe	Moderate	Mild	Total	ABC/3TC/LPVr	ABC/3TC/EFV	4dT/3TC/EFV	Other	Total
< 1 year	11	11	6	28	5	3	0	27	35
1- < 2 years	15	3	8	26	4	7	3	24	38
2- < 3 years	10	2	7	19	2	3	5	16	26
3- < 4 years	5	3	1	9	1	1	15	3	20
4- < 5 years	7	6	3	16	0	3	9	10	22
5 - < 10 years	10	5	5	20	0	1	16	10	27
Total	58	30	30	118	12	18	48	90	168
%age	49.2	25.4	25.4		7.1	10.7	28.6	53.6	
	Period: 2010-2014:					Period: 2010-2014:				
< 1 year	0	13	19	32	46	3	2	17	68
1- < 2 years	5	10	7	22	32	3	2	8	45
2- < 3 years	2	5	14	21	11	6	1	10	28
3- < 4 years	3	6	12	21	2	22	3	2	29
4- < 5 years	1	5	15	21	4	23	6	6	39
5 - < 10 years	28	38	15	81	3	66	27	24	120
10 - 13 years	5	9	3	17	0	18	0	2	20
Total	44	86	85	215	98	141	41	69	349
%age	20.5	40	39.5		28.1	40.4	11.7	19.8	
	Period: 2015-2019:					Period: 2015-2019:				
< 1 year	1	2	11	14	24	1	0	7	32
1- < 2 years	0	2	7	9	23	1	0	2	26
2- < 3 years	1	1	3	5	11	3	0	2	16
3- < 4 years	0	3	4	7	2	4	0	2	8
4- < 5 years	8	14	15	37	0	7	0	0	7
5 - < 10 years	1	12	7	20	3	39	1	7	50
10 - 13 years	0	0	1	1	1	21	0	1	23
Total	12	36	48	103	64	76	2	20	162
%age	11.7	35	46.6		39.5	46.9	1.2	12.3	

Key: CD4 count: Severe = <15%, Moderate = 15-24 % & Mild = ≥ 25%. Antiretroviral (ARV)-drugs: ABC = Abacavir, 3TC = Lamivudine, LPVr = Lopinavir+rotinavir, EFV = Efavirenz, 4dT = Stavudine.

were children < 3 years of age (30.5%), in the next policy period of 2010-2014, only 20.5% of patients presented with severely suppressed CD4 counts, with the majority being children 5 to <10 years of age (13%). The proportion of children < 3 years of age with severe CD4 count dropped to 3.3%. The same trend was observed in the policy period 2015-2019.

Regarding viral load testing, a similar trend in CD4 count was observed during each of the three policy periods. There were more children below 2 years with severe viral load (> 1000 copies/ml) than in the other age groups. The children under 2 years accounted for 37.5%, 54.2% and 35% of children with severe viral load in the respective policy periods. A viral load > 1000 implies severe or uncontrolled infection.

Table 4: The number and proportion (%) of patients with pulmonary tuberculosis (PTB) or pneumonia (PNM) in each age-group at the time of initiation of antiretroviral therapy (ART) during each policy period

Comorbid disease	Patients with Tuberculosis	(%)	Patients with Pneumonia	(%)
Period: 2004-2009				
< 1 year	14	32.6	3	20.0
1- < 2 years	6	14.0	6	40.0
2- < 3 years	6	14.0	4	26.7
3- < 4 years	3	7.0	1	6.7
4- < 5 years	8	18.6	0	0.0
5 - < 10 years	6	14.0	1	6.7
10 - <14 years	0	0	0	0
Total	43	100	15	100
%age	25.6		8.9	
Period: 2010-2014				
< 1 year	3	4.9	10	37.0
1- < 2 years	10	16.4	6	22.2
2- < 3 years	8	13.1	2	7.4
3- < 4 years	5	8.2	2	7.4
4- < 5 years	5	8.2	1	3.7
5 - < 10 years	25	41.0	5	18.5
10 - <14 years	5	8.2	1	3.7
Total	61	100	27	100
%age	17.5		7.7	
Period: 2015-2019				
< 1 year	4	17.4	3	25.0
1- < 2 years	7	30.4	1	8.3
2- < 3 years	1	4.3	3	25.0
3- < 4 years	1	4.3	0	0.0
4- < 5 years	0	0.0	1	8.3
5 - < 10 years	7	30.4	3	25.0
10 - <14 years	3	8.7	1	8.3
Total	23	100	12.	100
%age	14.2		7.4	

3.3. Prescribing

The most common ARV drugs on which patients were initiated were abacavir (ABC), azidothymidine (AZT), stavudine (4dT), Lamivudine (3TC), Efavirenz (EFV), and lopinavir+ritonavir (LPVr). Table 3 (Part 3B) shows the number of patients in each age group that were initiated on the recommended regimens in the HIV guidelines of the respective policy periods. In the policy period 2004-2009, the most commonly prescribed ART regimens were 'others' (regimens not recommended by national guidelines) at 53.6%, followed by the stavudine based regimen (d4T/3TC/EFV; 28.6%) for children ≥ 3 years old. In the period of 2010-2014, the utilization of 'others' and the stavudine regimens dropped to 19.8% and 11.7% respectively. This was associated with increased use of the ABC/3TC/LPVr regimen in children < 3 years, and the ABC/3TC/EFV regimen in children ≥ 3 years. By 2016, the stavudine regimen had been eliminated.

4. Discussion

In this paper, the characteristics of children with HIV who were initiated on ARV treatment at the five HIV-clinics in Bloemfontein, and their subsequent clinical management were described. The study highlights five important issues in the management of HIV in children in South Africa: (1) the status of implementation of the HIV treatment guidelines in pediatric patients at the primary health care level; (2) the reduced incidence of HIV infection in children; (3) the severe presentation of HIV infection in children; (4) the increased prevalence of HIV in school-age children; and (5) the exposure of many children to ARV drugs. Whereas the study period was over 15 years, the assessment of data over three periods (policy periods) of implementation using the National HIV treatment guidelines enabled an appropriate observation of the impact of each guideline. The management of HIV in children was guided by the treatment guidelines which, in addition to the provision of ART, included contact tracing and support beyond the clinic visit. The fact that this data extends beyond 2016 makes it very relevant to the current practice and challenges associated with the management of HIV in children, as expressed in a recent global health report.[12]

The study demonstrated that, although the ARV-roll out program began in 2004, under the 2004 national guidelines for the management of HIV,[13] it was not until 2010 that a significant number of pediatric patients were initiated on ARV therapy. This may be as a result of the 2004 guidelines which restricted the use of ARV drugs because it had a complex medical and psycho-social criterion for starting ART. The latter

was then followed by the release of the improved HIV/AIDS management guidelines in 2010 along with their subsequent revisions in 2013 and 2015 (sign of responsiveness) in which ARV drugs were made available to all people living with HIV regardless of age, CD4 cell count and clinical stage, and that initiation of ARV treatment should be prompt, preferably within 7 days of diagnosis. [1,14-16] These updates in the ART guidelines recognized that early pediatric HIV diagnosis is critical to timely initiation of ARV therapy to reduce morbidity and mortality, as well as guiding decisions on improving child nutrition and quality of life.[15-16] The guideline updates also included a change in the ARV drug regimens to the more effective ABC-based regimens, leading to the phasing out of the stavudine, dindanosine and azidothymidine based regimens due to drug toxicity and/or resistance. The preferred first-line regimens for initiation ARV therapy in children are ABC/3TC/LPVr for children less than 3 years, and ABC/3TC/EFV for children > 3 years. As indicated in this study, healthcare workers at the five ARV-clinics implemented the new guidelines appropriately.

The study also demonstrated a drastic drop in the number of children initiated on ARV therapy (new HIV cases) after 2016. This auger well with the implementation of the far-reaching guidelines in 2010 and 2015 as stated earlier. However, given that over 35.9% of the study sample were children under 2 years of age, the drop in new HIV cases at the clinic would relate more to the success of South Africa's prevention of maternal to child transfer (PMTCT) program.[17]

The high number of children below 2 years of age makes it difficult to interpret the data because there is no reliable data on the incidence and/or prevalence of HIV in children under 2 years of age. This population is almost always excluded from important surveys that produce these benchmarks. Specifically, in the 2017 South African National HIV Prevalence, Incidence, Behavior and Communication Survey (SABSSM study) only children 2-14 years old were included, yet the prevalence is quoted as for 'HIV in children' instead of in 'HIV in children 2-14 years.'[18] Using this same approach, it has been reported in all study resources or publications that the prevalence of 'HIV in children' in South Africa was 5.6% in 2002, 3.3% in 2005, 2.5% in 2008, 2.4%

in 2012 and 2.7% in 2017, yet all these reference reports excluded children below 2 years of age.[18]

This study showed that HIV infection was more severe in children under 2 years of age as they exhibited a lower weight for age that was below the 3rd percentile, severe disease at WHO-stages 3 and 4, significant immune suppression as indicated by a low CD4% (< 25%) and a high viral load of > 1000 copies/ml, and were at more risk of TB and opportunistic infections (OI). It also showed that from the start of ARV therapy, this age group was already in a poorer clinical state. It appears that most of the children were lost during the waiting period for confirmatory testing before initiation of treatment and their condition worsened.[19-20] This calls for a different approach to HIV care in children.

There is a need to modify the current guidelines on the management of children born of HIV-positive mothers.[21] The waiting period for confirmatory testing before initiation of treatment must be removed. It would be appropriate to regard all children born of HIV-positive mothers as HIV infected until proven otherwise. As such, they should be started on ARV drug treatment immediately (or within 7 days) and continue until 2 years of age or until it is proven that they are HIV-negative and have stopped breastfeeding. At 2 years of age or soon after, the ARV therapy can be interrupted for six months for confirmatory testing. As illustrated here, the fear for drug toxicity due to prolonged ARV drug exposure, particularly in the few who may be HIV- negative, is outweighed by the impact of the disease in the majority of this age group. This view is supported by recent reports, one on the Mississippi child in the USA, and the other, on a South Africa child where aggressive ARV treatment soon after birth leads to prolonged suppression of the virus.[22-23] In an earlier South African study, it was demonstrated that children who were started on ARV treatment within 12 weeks of life had better outcomes than those who started later.[24] In fact, in the 2010 WHO recommendations for a public health approach to ARV therapy in infants, the recommended age for immediate initiation of ARV drug therapy was "infants and children < 2 years."[25]

In this study, the high number of new infections observed in older children (> 5 years) implies that these children are contracting HIV from the community. There is therefore a need to come up with strategies to protect school children from behaviors that promote HIV infection and to actively search for children living with HIV for diagnosis and prompt treatment.

4.1. Strengths and Limitations of the study

The weakness of this study emanates from the fact that it is a retrospective study in which some information was not available and the small sample size. However, because the issues identified in this study on the severity of HIV in children less than 2 years provide further evidence to the views of some experts in the WHO,[3,25] these findings are relevant. Equally important is that these findings require urgent attention by the relevant authorities caring for children living with HIV, particularly in resource-limited countries.

5. Conclusion and Global Health Implications

In conclusion, the study established that more children were started on ART and safer ARV drugs. Children under 2 years were the most debilitated by HIV, and there was an increase in HIV prevalence among children > 5 years. New strategies for the prevention and management of HIV among children in these two age groups are needed.

Compliance with Ethical Standards

Key Messages

► The progressive updates and appropriate implementation of ART guidelines resulted in more children on ART, early initiation, and use of safer ARV drugs.

► Children under 2 years of age were the most afflicted by HIV infection.

► There was an increase in the prevalence of HIV infection in school children (> 5 years) within the study period.

► New strategies for prevention and management of HIV in children less than 2 years and school children are needed.

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