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ORIGINAL ARTICLE

Analysis of Morbidity and Mortality Factors among HIV-Infected Children in the Communal Medical Centres of the Municipality of Ratoma

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Abstract

Introduction: The objective of this study was to analyse the morbidity and mortality factors of HIV-infected children.

Material and Methods: This was a 10-year retrospective study from 1 January 2012 to 31 December 2021. All children aged 0-15 years with a positive HIV serological test or PCR under antiretroviral treatment and having a medical file were followed up in the two CMCs of the Ratoma commune.

Results: We collected 183 records of HIV-infected children on antiretroviral treatment. The median age was 3 years with extremes of 2 months and 15 years. More than half (60.1%) were <5 years old. More than half of the children (65.1%) were at WHO clinical stage (3 and 4). 60.8% had anemia with a median hemoglobin level of 10.7 g/dl. Respiratory diseases (39.34%) were the most common morbid events. Almost half (44.3%) were alive and followed up, 17.5% died, 23.5% lost to follow-up and 14.8% transferred. Anemia (18.75%) was the most common cause of death. Maternal non-education (p = 0.001), very low income (p = 0.0001), clinical screening (p = 0.0003), severe immunodepression (p = 0.002), tuberculosis (p = 0.007), clinical stage 3 (p = 0.0001) were the main risk factors associated with deaths.

Conclusion: The application of the new WHO recommendations for medical management, which require early initiation of antiretroviral treatment, the improvement of PMTCT performance and the promotion of systematic screening are necessary to reduce the morbidity and mortality of HIV-infected children in our context.

Introduction

Human immunodeficiency virus infection is a major public health problem worldwide, particularly in low- and middle-income countries [1].

According to UNAIDS, 37.7 million people were infected with HIV in 2020, including 1.7 million children under 15 years of age. In the same year, there were 150,000 new infections among children, including 2,300 in Latin America, 55,000 in West and Central Africa and only 35% of

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children in this region had access to antiretroviral treatment [2].

HIV progressively destroys the immune cells, thus preventing the normal functioning of immunity and the infected person progressively falls into a situation of immunodeficiency [3].

Mother-to-child transmission of HIV remains the primary voice of infection in children with a high morbidity and mortality rate in those under the age of 5 years [4]. Thus, in 2017, 76,000 young children (0-4 years) died from AIDS-related causes [5].

This study aimed to Analyse the factors associated with morbidity and mortality in children with HIV.

Methods

This study was conducted in the pediatric department of the Donka National Hospital (Conakry). It was a 10-year retrospective cross-sectional study from January 1, 2012 to December 31, 2021, including all HIV-infected children aged 0-15 years followed up in one of the two CMCs of Ratoma during this period.

The commune of Ratoma is one of the 5 communes of the city of Conakry, capital of the Republic of Guinea. Guinea, a West African country, is a low-income country with 44.8 per cent of the population having an income of less than $1.9 per day.

We included all children aged 0-15 years with a positive HIV serological test or PCR under ARV treatment who had a medical record and were followed up in one of the two CMCs. For each file, the parameters studied were: Age, gender clinical and biological characteristics.

Data were collected from the Kobo Collect application and then exported to Excel for cleaning and analysis using SPSS version 21 software. Data entry and presentation were performed using the Office 2016 pack. The calculation of frequencies allowed us to describe the qualitative variables. The distribution of quantitative variables was described by the median and extreme values.

Chi2 or Fisher tests were used to search for associated factors followed by multivariate logistic regression. The expected threshold for significance was set at $p < 0.05$. Our results were presented in tables and figures. The anonymity and confidentiality of the information collected were preserved.

We collected 183 records of HIV-infected children on antiretroviral treatment out of a total of 358 enrolled, i.e., a follow-up rate of 51.12%. Thus, nearly half of the files could not be found or were not usable, demonstrating the inadequacy of the health information system related to this service offer.

The nutritional status of the children was assessed using the weight-for-height ratio. Children with a weight-for-height ratio between -2 and -3 Z score were considered to be moderately malnourished and those with a weight-for-height ratio below -3 Z score were considered to be severely malnourished.

Wz used the WHO organisation classification to give the clinical stage taking into account the presenceof opportunist infections and he clinical evaluation of the patients.

The economic level of the families was determined according to the number of rooms in the home, the work of both parents and the number of people dependent on the household.

A working protocol was drawn up and validated by the university hospital authorities.

Informed consent was obtained from the parents for hildren under and the consent for children over 15 years old.Before data collection.

Results

We registered 183 HIV-positive children. The median age was 3 years with extremes of 2 months and 15 years. There were 83 (45.4%) boys and 100 (54.6%) girls, i.e. a sex ratio of 0.83 in favor of girls. 156 children came from Conakry (85.2%). 108 children were not orphans (59%) and 21 were orphans of both parents (11.2%).

One hundred and fourteen children had good nutritional status (62.3%), 28 had moderate malnutrition (15.3%) and 5 had severe malnutrition (2.7%). Nutritional status was not assessed for 27 children (19.7%). 6 children were in pediatric clinical stage 1; 49 (26.8%) in stage 2; 28 in stage 3 (15.3%) and 4 in stage 4 (1.6%). For 36 (19.7%) children the clinical stage had not been assessed. The median hemoglobin level was 11.5 g/dl with extremes of 6.4 and 12.7 g/dl.

The median viral load was 250 copies/ml with a median of 1 and 5454000 copies/ml.

Bronchopulmonary and ENT infections were the most common intercurrent diseases with 72 cases (39.3%) followed by bacterial skin infections (40 children or 21.86%).

Discussion

As this study was a retrospective study, the main limitation was that some médical records were incomplete.

During this work, we registered 183 cases of HIV-infected children on antiretroviral treatment out of a total of 358 enrolled, i.e. a follow-up proportion of 51.12%.

The median age was 3 years with extremes ranging from 2 months to 15 years. More than half had an age <5 years at initiation. This result is similar to that of Hmadou K [6] in Morocco who reported a median age of 3 years. On the other hand, Ngwej DT, et al. [7] in Congo and Diouf JBN, et al. [8] in Senegal found median ages of more than 5 years, including 9 and 8 years respectively. These results demonstrate the late detection of HIV in children despite the existence of a PMTCT program.

Females were predominantly represented with a sex ratio of 0.83 (Table 1). In contrast, a study conducted by Diemer H, et al. [9] in the Central African Republic found a predominance of males (53.2%).

This study showed that 33.9% of children were enrolled in school. Kalla GCM, et al. [10] in Cameroon reported a higher enrollment rate of 71%. This result

Table 1: Distribution according to socio-demographic characteristics associated with the occurrence of death of 183 children followed up in the two communal medical centers of the commune of Ratoma.

Variables	Dead				
	No		Yes		*p*-value
	N	%	N	%	
Age					
0 - 4	94	85.45%	16	14.55%	0.095
5 - 10	38	77.55%	11	22.45%	
11 - 15	19	79.16%	5	20.83%	
Sex					
Female	81	81%	19	19%	0.696
Male	70	84.34%	13	15.66%	
Vital status of parents					
No orphans	92	85%	16	15%	0.254
Motherless	17	71%	7	29%	0.106
Fatherless	25	83%	5	17%	0.897
Orphan of both parents	17	81%	4	19%	0.841
Person responsible for the child					
Father	41	82%	9	18%	1
Mother	64	85.33%	11	14.67%	0.435
Tutor	46	79.31%	12	20.69%	0.368
Niveau d'instruction de la mère					
None	56	73.68%	20	26.32%	0.01
Primary	15	93.75%	1	6.25%	0.312
Secondary and above	32	91.43%	3	8.57%	0.143
Unknown	48	85.71%	8	14.29%	0.53
Parents' economic situation					
High income	13	92.86%	1	7.14%	0.469
Average income	35	97.22%	1	2.78%	0.006
Low income	44	83.02%	9	16.98%	1
Very low income	3	20	12	80	< 0.0001
Unknown income	56	86.15	9	13.85	0.417

could be explained by the fact that the majority of the children in our study were under school age.

Forty point one percent (40.1%) of children were orphaned by at least one parent (Table 1). This rate is higher than the 37.8% found by Dicko-Traoré F, et al. [11] in Mali. Indeed, the loss of a parent could increase the vulnerability of the child who would be deprived of the support and love of his or her parents and consequently affect his or her medical care. This corroborates the data in the literature which states that in 2020, 15,400,000 children worldwide lost at least one parent to AIDS-related causes [12].

The children were cared for by one of the two parents in 68.3% of cases. Our result corroborates that reported by van Dijk JH, et al. [13] reported in Zambia that, 78.4% of children were cared for by one of the two parents. This could be explained by the high rate of parental death in our context.

At the initiation of treatment, serological testing was the most common diagnostic method used (82.0%).

The most common circumstance of discovery was clinical screening (60.1%) (Table 2). This result is similar to that of Barry MC, et al. [14] in Guinea who reported that 65.30% were detected during a consultation. This could be explained by the late detection of children.

More than half (58.5%) of the children had moderate and/or severe malnutrition (Table 3). This result is similar to that of Mwadianvita CK, et al. [15] in the DRC who reported an overall malnutrition of 60.2% including 8.4% severe malnutrition. This high prevalence of malnutrition at initiation could be explained by the fact that during the course of HIV, energy needs are greater while the virus acts on

Table 2: Distribution of 183 HIV-positive children followed according to clinical and biological characteristics at treatment initiation associated with the occurrence of death in the two communal medical centers of the commune of Ratoma.

Variables	Dead				
	No		Yes		
	N	%	N	%	*p*-value
Circumstances of discovery					
Clinical screening	82	74.55%	28	25.45%	0.0003
Prevention of mother-to-child transmission	28	90.32%	3	9.68%	0.3
Intra-family screening	40	97.56%	1	2.41%	0.002
Systematic screening	1	100%	0	0%	1
WHO clinical stage					
Stage I	40	97.56%	1	2.44%	0.002
Stage II	21	91.30%	2	8.70%	0.377
Stage III	71	77.17%	21	22.83%	0.078
Stage IV	19	70.37%	8	29.63%	0.096
Nutritionnal status					
Good nutritional status	67	88.16%	9	11.84%	0.204
Moderate malnutrition	55	79.71%	14	20.29%	
Severe malnutrition	29	76.32%	9	23.68%	
Hemoglobin level (g/dl)					
Median (extremes)	10.7(6-14.3)		10.7(4-12)		0.305
Treatment regimen					
ABC+3TC+EFV	16	80%	4	20%	0.754
ABC+3TC+LPVr	33	91.67%	3	8.33%	0.107
Autre	2	50%	2	50%	0.083
AZT+3TC+LVPr	6	85.71%	1	14.29%	0.82
AZT+3TC+NVP	78	83.87%	15	16.13%	0.623
TDF+3TC+EFV	7	77.78%	2	22.22%	0.701
D4T+3TC+NVP	9	64.29%	5	35.71%	0.062

NVP: Névirapine; EFV: Efavirenz; LVP: Lopinavir; 3TC: Lamivudine; AZT: Zidovudine; ABC: Abacavir; D4T: Stavudine; TDF: Tenofovir

Table 3: Distribution of 183 HIV-positive children followed up according to clinical characteristics during the follow-up associated with the occurrence of death in the two medical communal centers of Ratoma commune.

Variables	Dead				
	No		Yes		
	N	%	N	%	*p*-value
WHO Clinical Stage					
Stage I	67	100%	0	0%	< 0.0001
Stage II	44	89.79%	5	10.20%	0.13
Stage III	15	53.57%	13	46.43%	< 0.0001
Stage IV	1	33.33%	2	66.67%	0.079
Not rated	24	66.67%	12	33.33%	0.012
Nutritional status					
Good nutritional status	105	92.11%	9	7.89%	< 0.0001
Moderate malnutrition	20	71.43%	8	28.57%	0.107
Severe malnutrition	2	40%	3	60%	0.038
Not rated	24	66.67%	12	33.33%	0.012
Hemoglobin level (g/dl)					
Médian (extremes)	11.2(6.4-12.7)		9.7(8.1-11.7)		0.014

the metabolism and consequently deteriorates the nutritional status [16].

More than half of the children (65.1%) were at WHO clinical stage (3 and 4). Severe immunosuppression was the most represented immunological stage (Table 4). The predominance of clinical stage 3 or 4 and advanced or severe immunological stage was also found in other studies conducted in sub-Saharan Africa; such as Edmond A, et al [17] in the Democratic Republic of Congo, Takassi OE, et al. [18] in Togo, Kalla GCM, et al. [10] in Cameroon. These results reflect the late management of HIV in children in resource-limited countries.

There were 60.8% of children with anemia with a median hemoglobin level of 10.7 g/dl. A similar result was reported by Mwadianvita CK, et al. [19] in Congo, i.e. 69.1%. This high rate of anemia in our context could be explained by the fact that the majority of children consulted at an advanced clinical stage with malnutrition likely to lead to anemia.

After one year of treatment, a clinical and biological improvement was observed. In particular, good nutritional status in more than half of the children (62.3%), clinical stage1 in (36.61%), absence of immunosuppression in 26.8% of cases. More than half (52.9%) had a hemoglobin level (>10 g/dl) and almost half (43.5%) had an undetectable viral load (<50 copies/ml). A better improvement in clinical and biological status was found by Ngwej DT, et al. [6] in Congo who found during the evaluation of the management of children under antiretroviral treatment WHO clinical stage 1 (75.8%) absence of immunosuppression (72.6%), hemoglobin level ≥8 g/dl (98.3%), undetectable viral load (67.7%). The effectiveness of antiretroviral treatment could explain these results.

Bronchopulmonary disease (39.34%), ENT disease (39.34%), followed by bacterial skin disease (21.86%) and gastroenteritis (20.77%) were the most common morbid events found in children during follow-up. These results are similar to those of Touré A, et al. [20] in Togo who found that the most common morbid events were pneumonia (37.1%) and gastroenteritis (11.3%). On the other hand, Kobangué L, et al. [4] reported anemia as the main disease encountered (75.8%).

Twenty-two percent (20.2) of children were hospitalized (Table 5). Our results are different from those of Touré A, et al. [20] in Togo who found a hospitalization rate of 3.1%.

The most commonly used treatment regimen at initiation was AZT+3TC+NVP (50.8%). On the other hand, in the study by Kalmogho A, et al. [21] in Burkina Faso, the most commonly used treatment regimen was D4T+3TC+NVP with a proportion of 42.11%. This result could be explained by the fact that in our country, AZT+3TC+NVP is a first line regimen in children [22].

Table 4: Multivariate logistic regression of variables at treatment initiation associated with the occurrence of death in the 183 children followed in the two communal medical centers of Ratoma commune.

Variables	Coefficient	OR	IC-95%	*p*-value
Niveau d'instruction de la mère				
None	0.41	0.47	0.47-4.50	0.490
Parents' economic situation				
Average Income	-1.83	2.73	0.02-1.40	0.098
Very low income	2.99	9.10	2.86-140.1	0.003
Circumstances of discovery				
Clinical screening	-.511	0.229	0.07-4.87	0.632
Intra-family screening	-2.19	2.39	0.00-1.80	0.122
WHO clinical stage				
Stage I	-2.90	3.58	0.00-1.11	0.058
Immunological stage				
Severe ID	0.707	1.078	0.53-7.70	0.299

Table 5: Distribution of 183 HIV-positive children followed up according to therapeutic and evolutionary characteristics in the two communal medical centers of the commune of Ratoma.

Variables	Number	Proportion (%)
Treatment regimen at initiation		
ABC+3TC+EFV	20	10.9%
ABC+3TC+LPV/r	36	19.7%
AZT+3TC+LVP/r	7	3.8%
AZT+3TC+NVP	93	50.8%
TDF+3TC+EFV	9	4.9%
D4T+3TC+NVP	14	7.65%
Other	4	2.18%
Cotrimoxazole prophylaxis		
No	1	0.5%
Yes	182	99.5%
Hospitalization		
No	146	79.8%
Yes	37	20.2%
Evolution		
Dead	32	17.5%
Lost to view	43	24.5%
Transferred	27	14.8%
Living and monitored at the Centre	81	44.3%
Causes of death		
Anemia	6	18.75%
Severe pneumonia	5	15.62%
Tuberculosis	5	15.62%
Acute gastroenteritis	3	9.37%
Severe malnutrition	2	6.25%
Renal insufficiency	1	3.12%
Other	3	9.37%
None	8	25%

NVP: Nevirapine; EFV: Efavirenz; LVP: Lopinavir; 3TC: Lamivudine; AZT: Zidovudine; ABC: Abacavir; D4T: Stavudine; TDF: Tenofovir

Cotrimoxazole prophylaxis was observed in almost all children (99.5%). Our result is similar to that of Takassi A, et al. [18] who found 99% of children on cotrimoxazole prophylaxis.

During follow-up, we found that almost half (44.3%) were alive and followed up, 17.5% died, 23.5% lost to follow-up and 14.8% transferred.

In addition, 50% of the cases of death involved children under 5 years of age. A different result was found by Koueta F, et al. [23] in Burkina Faso who reported 18.5% of deaths with 75% of infants.

Anemia (18.75%) was the most common cause of death followed by severe pneumonia and tuberculosis with a common proportion of 15.62%. However, the cause of death was unknown in 25% of cases. Kalmogho A, et al. [21] found that the cause of death was unknown in 60% of the cases and the most common probable causes of death were respiratory infections of common pneumonia (10%) and tuberculosis (5%). This high rate of death due to anemia could be explained by the fact that in our study 60.8% of children were anemic at initiation.

Regarding the socio-demographic characteristics we found an association between the mother's lack of education, very low income and the occurrence of death with significant differences of ((p = 0.010), (p < 0.0001)) respectively. On the other hand, there was no significant difference between the occurrence of death and age (p = 0.095), gender (p = 0.696). Van Dijk JH, et al. [13] in Zambia showed an association between younger age and death (p = 0.001). Kalla GCM, et al. [10] also showed an association between age and survival of HIV infected children (p < 0.0001) (Table 1).

At initiation, the circumstances of clinical (25.45%) and intra-family (2.41%) screening were related to the occurrence of death with significant differences (p = 0.0003), (p = 0.002) respectively. This explains the interest of early diagnosis and screening of all family members of persons followed for HIV infection without waiting for the occurrence of a pathological episode.

The WHO clinical stage 1 (2.44%) and severe immunodepression (37.14%) were also significantly associated with the occurrence of death with for each (p = 0.002). Furthermore, the association of death with WHO clinical stage (3 and 4) p = 0.048 and severe immunodepression (p = 0.029) were found in the Gebremedhin A, et al. [24] study in Ethiopia; Takassi OE, et al. [25] in Togo reported that the occurrence of death was related to WHO clinical stages 3 and 4 in 70% of cases with a highly significant difference (p = 0.0003) and to severe immunodepression with a significant difference (p = 0.0038). This could be explained by the fact that the WHO recommendations of early diagnosis and treatment of HIV-infected children are not met in all cases [26]. Early diagnosis and treatment could have prevented progression to an advanced clinical or immunological stage and therefore decreased mortality in these children.

We found that digestive candidiasis (p = 0.043) and tuberculosis (p = 0.007) were significantly associated with the occurrence of death. All opportunistic infections, Kalla GCM, et al. [10] in 2018 also demonstrated an association between opportunistic infections and survival in HIV-infected children with a p < 0.0001.

After one year of follow-up, the clinical and biological characteristics associated with the occurrence of death were clinical stage I (p < 0.0001) found in no case of death, clinical stage III (p < 0.0001) found in 46.43% of deaths; non-assessment of clinical stage (p = 0.012) of which 33.33% died, severe immunodepression (p = 0.018) in 57.14% of deaths, good nutritional status (p < 0.0001) in 7.89% of deaths; severe malnutrition (p = 0.038) in 60% of cases, non-assessment of nutritional status (p = 0.012) of which 33.33% died, haemoglobin level (p = 0.014). Therefore, an improvement of the clinical and biological status in all children at one year of treatment could have significantly decreased this high mortality (Table 6).

Hospitalization was associated with the occurrence of death with a highly significant difference (p < 0.001). A similar result was found by Touré MA, et al. [20] in Togo who reported an association between hospitalization and death with a (p < 0.001) (Table 7).

In multivariate analysis, we found that there was a statistically significant correlation between the risk of death and very low income (p = 0.003). The lower the income the higher the risk of death (OR = 9); (2.86-140.16). In other words, children whose parents or guardians had very low income were nine times more likely to die than those who did not.

The link between socioeconomic level and death is a recognized phenomenon in our country. For example, in the 2018 DHS, the risk of death for children was three times higher in the first two lowest

Table 6: Distribution of 183 HIV-positive children monitored according to intercurrent diseases associated with the occurrence of death in the two CMCs of Ratoma commune.

Variables	Dead				
	No		yes		*p*-value
	N	%	N	%	
Bronchopulmonary conditions	58	80.56%	14	19.44%	0.422
Scabies	12	70.59%	5	29.41%	.174
Otorhinolaryngology conditions	62	86.11%	10	13.89%	0.54
Digestive candidiasis	5	55.56%	4	44.44%	0.043
Gastroenteritis	31	81.58%	7	18.42%	0.806
Bacterial skin infections	34	85%	6	15%	1
Viral skin infections	3	75%	1	25%	0.52
Skin mycoses	15	83.33%	3	16.67%	1
Malaria	21	91.30%	2	8.70%	0.376
Parotiditis	2	100%	0	0	1
Measles	5	100%	0	0	0.591
Infectious Syndrome	2	66.67%	1	33.33%	0.423
Tuberculosis	4	44.44%	5	55.56%	0.007
None	38	86.36%	6	13.64%	0.645
Auther	25	80.64%	6	19.35%	0.415

Table 7: Results of multivariate logistic regression of clinical and biological characteristics during follow-up associated with the occurrence of death in the 183 children followed in the two communal medical centers of Ratoma commune.

Variables	Coefficient	OR	IC-95%	*p*-value
Tuberculosis	-3.043	1.820	.001-3.968	0.177
Stage 1	21.639	0.000	0.000	0.997
Stage 3	-2.213	1.727	0.004-2.965	0.189
Severe ID	-4.598	3.454	0.000-1.285	0.063
Good nutritional status	0.968	0.541	0.199-34.677	0.462
Taux d'hémoglobine	-2.150	3.853	0.013-.996	0.050
Hospitalization				
yes	-1.823	4.332	0.029-0.899	0.037

quintiles of economic well-being than in the highest [27].

Conclusion

HIV infection remains a major public health problem. Maternal non-education, very low parental income, clinical screening, severe immunosuppression, tuberculosis, and WHO clinical stage 3 were the main risk factors associated with the occurrence of deaths. We recorded a significant proportion of deaths with anemia as the main etiology.

The application of the new WHO recommendations for medical management, which require the early initiation of antiretroviral treatment, the improvement of PMTCT performance and the promotion of systematic screening are necessary to reduce the morbidity and mortality of HIV-infected children in our context.

Conflicts of Interest

The authors declare that there are no conflicts of interest

Author Contributions

All authors contributed significantly to the research and development of this scientific article.

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