HIV Prevalence and Impact on Renutrition in Children Hospitalised for Severe Malnutrition in Niger: An Argument for More Systematic Screening

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Abstract

Background: In developing countries, malnutrition is a contributing factor in over 50% of child deaths. Mortality rates are higher in underweight children, and HIV-infection is known to increase underweight. Our goals were to evaluate the prevalence of HIV among children hospitalised for severe malnutrition (SM) at the Niamey national hospital (Niger), and to compare renutrition and mortality by HIV-status.

Methods: Retrospective study based on all children <5 years hospitalised for SM between January 1st 2008 and July 1st 2009. HIV-prevalence was the ratio of HIV+ children on the number of children tested. Duration of renutrition and mortality were described using survival curves.

Results: During the study period, 477 children were hospitalised for SM. HIV testing was accepted in 470 (98.5%), of which 40 were HIV+ (HIV prevalence (95% confidence interval) of 8.6% (6.2–11.5)). Duration of renutrition was longer in HIV+ children (mean: 22 vs. 15 days; p = 0.003). During renutrition, 8 (20%) and 61 (14%) HIV+ and HIV− children died, respectively (p = 0.81).

Conclusion: Around 9% of children hospitalised for severe malnutrition were HIV infected, while in Niger HIV prevalence in adults is estimated at 0.8%. This pleads for wider access to HIV testing in this population.

Introduction

In developing countries, malnutrition contributes to nearly 50% of deaths in children, although it may not be the direct cause of death [1]. In children, mortality is strongly related to body growth parameters represented by weight-for-height, weight-for-age and height-for-age z-scores. The risk of death was 10 fold higher in children with a weight-for-height z-score ≤−3 (severe wasting) when compared to children with a z-score higher or equal to −1 [2].

Malnutrition can be attributed to nutritional deficiency, still malnutrition is multi factorial and HIV-infection can also induce or aggravate it. In fact, wasting is a WHO stage 3 AIDS condition. This interaction between HIV infection and malnutrition is all the more important since areas of relatively high prevalence of both conditions often overlap in developing countries.

A study conducted in Malawi showed that mortality during renutrition was higher in HIV-positive children than in HIV-negative children [3,4]. But this study took place in a context of very high HIV-prevalence. Furthermore, it is not known whether children infected with HIV respond differently to renutrition than uninfected children, particularly in terms of duration of renutrition.

Very few studies have been conducted to study how the burden of HIV affects malnutrition in developing countries, and little is known about nutritional and clinical recovery of HIV-positive children. In this study, we aimed at estimating HIV prevalence in children hospitalised for severe malnutrition in a context of low HIV prevalence, and at comparing the recovery during hospitalisation in terms of weight gain and mortality.

Methods

Ethics statements

The protocol of this study has been submitted and approved by the Niger ethics committee (Comité Consultatif National d’Éthique). Patients’ consent was not asked for as the study was retrospective and data was entered in the database and analysed anonymously; the Niger ethics committee approved the waiver of consent.
This retrospective study enrolled all children aged 5 years or less hospitalised for severe malnutrition at the intensive therapeutic feeding centre (CRENA) of the Niamey national hospital (NNH) paediatric ward (Niamey, Niger). The study period was defined as January 1st 2008 to June 30th 2009 as it was expected to enable the enrolment of the number of children required to accurately estimate HIV-prevalence. Under the assumption that prevalence was 5%, to obtain a precision of $\pm 2\%$ with a type-I error of 5%, the number of children required was 457 (Nquery). Assuming a 90% acceptance of the HIV-test, 508 children were to be enrolled in the study.

For all children hospitalised for severe malnutrition during this period, information was extracted from the clinical files and made anonymous by using a unique identifier code and then filled in a standardised form. These forms were then recorded in a computerised database (Epi Info).

According to the national protocol and WHO recommendations, acute severe malnutrition was defined based on clinical signs (<70% weight for height or oedema of both feet and clinical signs of severe malnutrition) [5]. Clinical differential diagnosis was made between marasmus (global intake deficiency) characterized by severe and visible loss of weight and kwashiorkor (type 2 nutrient deficiency) mostly characterized by bilateral limb oedema. Some children may present both types of malnutrition. Finally, in children ≤6 months old, malnutrition was qualified as demeritition.

According to the national protocol, intensive renutrition lasts approximately 3 weeks in three phases: (i) acute phase of renutrition during which children, receive therapeutic milk F75 and lasts approximately 1 week; (ii) stabilisation phase during which children receive therapeutic milk F100 usually lasts around 3 days; (iii) consolidation phase of renutrition during which children receive therapeutic milk F100 and ready-to-use therapeutic food (RUTF) such as Plumpy'nut [6] during about 10 days. F75 and F100 are standardized therapeutic milks, specifically designed to treat severe malnutrition, and providing 75 and 100 kilo-calories per 100 ml, respectively [6]. Condition for discharge to the ambulatory nutrition rehabilitation unit (CRENA) was achieving a weight >85% of the weight-for-height standard in children with Marasmus or absence of complication in children with kwashiorkor.

HIV testing of the child was proposed routinely to all mothers who could accept or refuse the test. From January 2007, in children less than 18 months of age, amplification of the integrated viral genome by PCR was used to define the HIV status. HIV-positive children were referred to the HIV ward and were taken care of for free as proposed by the national programme.

Children’s characteristics were compared by HIV status using student t-test for continuous variables and chi-2 test for categorical variables. Factors associated with HIV status were identified using a univariate and then multivariate logistic regression model.

Duration of hospitalisation for renutrition was defined as the duration from the date of hospitalisation to the date of discharge, death, transfer to another hospital or the date when they left hospital against medical advice. Duration of hospitalisation was described by HIV status using a competing risk approach based on cumulative incidence, and considering death as a competing risk, while children who were transferred or left hospital against medical advice were considered as censored [7]. We used the Cox proportional hazard model to identify factors, other than HIV status, which were associated with the duration of hospitalisation for renutrition. The proportional hazard assumption was validated for all factors investigated using the test on Schoenfeld’s residuals.

Mortality during hospitalisation was described using Kaplan-Meier estimates, and was compared by HIV-status using the logrank test. Factors associated with mortality were identified using a parametric survival regression model with a log-normal distribution, as the proportional hazard assumption was not valid for some of the factors investigated.

In all multivariate analysis, factors associated with the event of interest with a p-value <0.2 in univariate analysis were entered in the multivariable model. Then, a backward procedure was applied to identify factors independently associated with the event of interest. All significance tests were two-sided and P-values less than 0.05 were considered statistically significant. All statistical analyses were performed using STATA 10 (Stata Corp., College station, Texas, USA).

Results

From January 1st 2008 to July 1st 2009, 473 children were hospitalised for severe malnutrition, corresponding to a mean of 26 children per month. HIV testing for the children was proposed to all mothers or care-givers and was accepted in 467 (98.7%) children.

Of the 467 children with an HIV test result, 40 were found to be HIV-positive corresponding to an HIV prevalence of 8.6% (95% confidence interval: CI: 6.2–11.5). HIV prevalence was significantly higher in girls than in boys (11.5% [95% CI: 7.6–16.4] and 6.0% [95% CI: 3.4–9.7], respectively; p = 0.03) (Table 1) Median age at hospitalisation was 13 months and was not different by HIV status. Of these children, 208 (44%) were aged ≤12 months, 195 (42%) were aged 13 to 24 months, 50 (11%) were aged 25 to 36 months and only 14 (3%) were aged more than 36 months. No difference between HIV-positive and negative children were found regarding the mother’s age and geographic origins defined as urban versus rural. Most children (59.5% and 70.0% among the HIV-negative and HIV-positive children, respectively; p = 0.20) presented Marasmus.

The weight-for-age z-score was very low both in HIV-negative and HIV-positive children, and was not statistically different in these two groups (Table 1, p = 0.75). The z-score indicated the severe wasting (93.6% with z-score ≤−3) of this population. As expected, z-score was significantly lower in children with marasmus than in children with kwashiorkor (p<0.001).

Height-for-age z-score was also low in this population, but again not different between HIV-negative and HIV-positive children (Table 1, p = 0.23). The proportion of children being stunted (z-score ≤−2) was 64.2%, and severely stunted (z-score ≤−3) was 38.7%.

A larger proportion of HIV infected children had a previous history of hospitalisation compared to HIV-negative children (30.0% versus 4.7%, respectively; p<0.001). When only previous hospitalisation for severe malnutrition was considered, the proportion remained significantly higher in HIV-positive children compared to HIV-negative children (15.0% versus 2.1%, respectively; p = 0.001).

Of the 467 children, 401 (85.9%) were referred by another hospital and 66 (14.1%) presented directly at the NNH paediatric ward (internal referral). HIV prevalence was found to be significantly higher in children from internal referral than from external referral [30.3% versus 5.0%, respectively; p<0.001].

Both in univariate and multivariate logistic regression analysis (table 2), female gender, previous hospitalisation (whether for renutrition or not) and internal referral were associated with a higher risk of HIV-positive status. None of the other factors investigated were associated with HIV status.

Of the 467 children, 363 (76.7%) were discharged to the ambulatory nutrition rehabilitation unit (CRENA), 79 (16.7%)...
died during renutrition, 26 (5.5%) left hospital against medical advice, and 5 (1.1%) were transferred to another hospital. Duration of hospitalisation was longer in HIV-positive children than in HIV-negative children (Figure 1). The probability of discharge to the CRENA at 3 weeks was 63% in HIV-negative children and 41% in HIV-positive children.

In a univariate Cox model all the factors presented in the table 2 were investigated. The rate of discharge to the CRENA was significantly lower in HIV-positive children when compared to HIV-negative children (crude hazard ratio (HR) [95% CI]: 0.44 [0.30–0.67]; p<0.001). It was consistent with the fact that the proportion of children who returned to phase 1 renutrition was larger in HIV-negative children (12.5% versus 3.0%, p = 0.03). Among all other factors investigated, only gastro-enteritis diagnosed at hospitalisation was associated with a higher rate of discharge to the CRENA. The rate of discharge being higher in children who presented this condition than in the children not presenting this condition (crude HR [95% CI]: 1.52 [1.17–1.98]; p<0.001). In multivariate analysis, HIV status and gastro-enteritis condition remained independently associated with the rate of discharge to the CRENA (adjusted HR [95% CI]: 0.44 [0.29–0.65] and 1.54 [1.19–2.01], respectively; both p<0.001).

Based on Kaplan-Meier estimates [figure not shown], mortality was not statistically different between HIV-positive and HIV-negative children (p = 0.97). All factors presented in the table 2 were investigated regarding their effect on mortality. The only factor significantly associated with mortality was a malaria diagnostic, the risk of dying for more than 5-fold higher in children with malaria than in children without (crude HR [95% CI]: 5.48 [1.67–17.98]; p = 0.003).

Only considering those children who were discharged to the CRENA, both HIV-negative and HIV-positive children gained weight (in median +17.0% and +20.4%, respectively; p = 0.92). Nevertheless, weight-for-age z-scores remained low in both groups.

The most common pathologies associated with malnutrition were pneumonia in 114 (24.3%) children, malaria in 112 (23.9%) children, and gastro-enteritis in 82 (17.5%) children (Table 1), and were as frequent in HIV-negative as in HIV-positive children (p = 0.93, p = 0.16, p = 0.19, respectively).

**Discussion**

This is one of the very few studies to estimate HIV prevalence in children hospitalised for acute severe malnutrition in West Africa. Indeed, a study in Nigeria reported in 1997 a HIV prevalence of 1.9% [8] while a study in Burkina Faso in 1993 reported a HIV prevalence of 14.0% [9]. Routine HIV testing of children hospitalised for severe malnutrition was implemented in 2006 at the NNH, and these results show an extremely high level of acceptance. Indeed, nearly 99% of the mothers accepted HIV testing for their children.

**Table 1. Children’s characteristics.**

|                      | HIV-negative (N = 427) | HIV-positive (N = 40) | p      |
|----------------------|-----------------------|----------------------|--------|
| **Demographic**      |                       |                      |        |
| Boys, N (%)          | 236 (55.3)            | 15 (37.5)            | 0.03   |
| Age in months, median (IQR) | 13 (9 ; 21)   | 16 (9 ; 24)         | 0.18   |
| Age of the mother in years*, median (IQR) | 26 (22 ; 30) | 28 (25 ; 34) | 0.10   |
| Urban versus rural, N (%) | 244 (56.9)        | 26 (65.0)            | 0.32   |
| **Clinical**         |                       |                      | 0.51   |
| Type of malnutrition |                       |                      |        |
| Marasmus             | 254 (59.5)            | 29 (72.5)            |        |
| Kwashiorkor          | 52 (12.2)             | 3 (7.5)              |        |
| Mixed form           | 65 (15.2)             | 3 (7.5)              |        |
| Denutrition**        | 56 (13.1)             | 5 (12.5)             |        |
| Previous hospitalisation | 409 (95.3)     | 28 (70.0)            | <0.001 |
| No                   | 409 (95.3)            | 28 (70.0)            |        |
| Yes, for malnutrition| 9 (2.1)               | 6 (15.0)             |        |
| Yes, for other reason| 11 (2.6)              | 6 (15.0)             |        |
| % of the normal weight for the height, median (IQR) | 67.0 (62.8 ; 71.0) | 66.5 (63.6 ; 71.2) | 0.50   |
| Weight-for-age z-score***, median (IQR) | -4.7 (-5.3 ; -3.9) | -4.7 (-5.5 ; -3.9) | 0.75   |
| Height-for-age z-score, median (IQR) | -2.4 (-3.6 ; -1.5) | -3.0 (-4.1 ; -1.6) | 0.23   |
| Main other diagnosis, N (%) |                  |                      |        |
| Anaemia              | 56 (13.1)             | 3 (7.5)              | 0.31   |
| Pneumonia            | 104 (24.2)            | 10 (25.0)            | 0.93   |
| Malaria              | 106 (24.7)            | 6 (15.0)             | 0.16   |
| Gastro-enteritis     | 78 (18.2)             | 4 (10.0)             | 0.19   |

*available in 417 and 38 mothers.

**this applies to children ≤6 months of age.

***available in 423 HIV-negative and 38 HIV-positive children.

IQR: inter quartile range.

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In this study, based on an exhaustive sample of 469 children hospitalised for acute severe malnutrition, HIV-prevalence was 8.5%. In Niger, no data on HIV-prevalence in children are available; HIV prevalence in adults is estimated at 0.8% [10], but in this population of children hospitalised for severe malnutrition, the HIV prevalence is nearly 10 fold higher. Thus, it is no longer possible to ignore that children hospitalised for severe malnutrition are a very high-risk population for HIV infection and our result pleads for implementation of routine HIV testing in nutrition rehabilitation units, as proposed by another recent study [11].

HIV prevalence was found to be significantly higher in children from internal referral (coming from the NNH) when compared to children from external referral (referred from a lower level health care facility). This result could suggest a selection bias due to the availability of a HIV-care centre in the NNH. However, it first should be noted that children from external referral represented 86% of our study population, and HIV-prevalence was 5% in these children, i.e. still around 7-fold that observed in adults. Secondly, admission in the CRENI was strictly based on nutritional status, whatever the origin of the children (internal or external reference), so that nearly no child should have been hospitalised in the

### Table 2. Risk factor of HIV-positive status (univariate and multivariate analysis).

|                                    | Crude OR (95% CI) | P   | Adjusted OR (95% CI) | P   |
|------------------------------------|------------------|-----|----------------------|-----|
| Gender                             |                  |     |                      |     |
| Male                               | 1                | 0.03| 1                    | 0.02|
| Female                             | 2.06 (1.06–4.02) |     | 2.48 (1.17–5.25)     |     |
| Age, months                        |                  |     |                      |     |
| ≤ 12                               | 1                | 0.49|                      |     |
| 13–24                              | 1.15 (0.56–2.33) |     |                      |     |
| 25–36                              | 1.04 (0.33–3.27) |     |                      |     |
| > 36                               | 3.27 (0.82–12.94) |    |                      |     |
| Age of the mother*, years          |                  |     |                      |     |
| ≤ 22                               | 1                | 0.35|                      |     |
| 23–27                              | 1.58 (0.56–4.50) |     |                      |     |
| 28–30                              | 2.12 (0.74–6.06) |     |                      |     |
| > 30                               | 2.31 (0.84–6.38) |     |                      |     |
| Reference                          |                  |     |                      |     |
| External                           | 1                | <0.001|                      | 1<0.001|
| Internal                           | 8.28 (4.15–16.53)|     | 7.90 (3.79–16.48)    |     |
| Geographical origin                |                  |     |                      |     |
| Urban                              | 1                | 0.32|                      |     |
| Rural                              | 0.71 (0.36–1.40) |     |                      |     |
| Prevalence of hospitalization      |                  |     |                      |     |
| No                                 | 1                | <0.001|                      | 1<0.001|
| Yes, not for malnutrition          | 7.93 (2.73–23.02)|     | 7.10 (2.24–22.51)    |     |
| Yes, for malnutrition              | 9.69 (3.22–26.16)|     | 8.68 (2.60–28.97)    |     |
| Type of malnutrition               |                  |     |                      |     |
| Marasmus                           | 1                | 0.46|                      |     |
| Kwashiorkor                        | 0.70 (0.23–2.07) |     |                      |     |
| Mixed form                         | 0.42 (0.12–1.42) |     |                      |     |
| Denutrition                        | 0.81 (0.30–2.19) |     |                      |     |
| Brachial perimeter<110 mm          |                  |     |                      |     |
| No                                 | 1                | 0.11|                      |     |
| Yes                                | 0.49 (0.25–0.99) |     |                      |     |
| Missing                            | 1.21 (0.24–6.03) |     |                      |     |
| Oedema of the feet                 |                  |     |                      |     |
| No                                 | 1                | 0.11|                      |     |
| Yes                                | 0.52 (0.22–1.21) |     |                      |     |
| Weight-for-age z-score             |                  |     |                      |     |
| ≤ -5                               | 0.74 (0.19–2.80) |     | 0.90                 |     |
| -4 and -3                          | 0.82 (0.23–2.89) |     |                      |     |
| ≥ -2                               | 1                |     |                      |     |
| Height-for-age z-score             |                  |     |                      |     |
| ≤ -3                               | 1.27 (0.49–3.32) |     | 0.67                 |     |
| -2                                 | 0.78 (0.26–2.35) |     |                      |     |
| -1                                 | 0.85 (0.27–2.65) |     |                      |     |
| ≥ 0                                | 1                |     |                      |     |
| Weight-for-height z-score          |                  |     |                      |     |
| ≤ -4                               | 0.53 (0.23–1.22) |     | 0.15                 |     |
| ≥ -3                               | 1                |     |                      |     |
| Malaria                            |                  |     |                      |     |
| No                                 | 1                | 0.15|                      |     |
| Yes                                | 0.53 (0.22–1.31) |     |                      |     |

*based on the 25th, 50th and 75th percentiles.

OR: odds ratio; CI: confidence interval.

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