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Co-infection of malaria and HIV infection in severely undernourished children in the Democratic Republic of the Congo: a cross-sectional study

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Research Article

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Abstract

Purpose. This study aims to determine the prevalence of malaria and HIV seropositivity among children with undernutrition in the Democratic Republic of the Congo.

Methods. A cross-sectional study of undernourished children aged between 12 and 60 months in Kalembe-Lembe hospital was carried out. Blood samples were collected for the analyses of malaria parasite, haemoglobin and haematocrit levels. HIV serostatus was determined with rapid HIV antibody tests and enzyme-linked immunosorbent assay. Logistic regression analyses were used to identify clinical predictors of HIV seropositivity.

Results. Of 225 children, 88.9% had malaria; the parasite loads were 16 000 para per μL (38.0%); 24 400 para per μL (56.8%), $P < 0.001$ and malaria and associated HIV infection accounted for 29.2%. In children aged >12 months, HIV seroprevalence was 29.3%; 86.0% had undernutrition and malaria, 6.8% had undernutrition and HIV and 4.3% had undernutrition, HIV and malaria ($P < 0.001$). The occurrence of at least three or more symptoms was highly specific (96.4–100.0%) for HIV seropositivity ($P < 0.05$). The overall mortality rate was 18.4%, higher in children with malaria and HIV (39.6% *vs* 12.2%, $P < 0.001$) and those with lower weight gain (4.3 *vs* 7.5 g kg^{-1} day^{-1}, $P < 0.001$).

Conclusions. There was high prevalence of malaria and HIV and mortality among severely undernourished children with malaria and HIV.

Introduction

Malaria, HIV/AIDS and undernutrition continue to plague many countries in the developing world, 2011. At the end of 2016, 3.4 million children under 15 years were estimated to be living with the virus globally and more than 90% of these were in sub-Saharan Africa (WHO, 2011). The Democratic Republic of the Congo (DR. Congo) continues to have a generalized HIV epidemic, with a national HIV prevalence of 2.5%; HIV and undernutrition are intricately interwoven. Clinically, unexplained severe wasting or severe undernutrition not responding to standard therapy is classified as stage IV in paediatric AIDS (WHO, 2007). Malaria, severe undernutrition and HIV have both been known to have a deleterious effect on the immune system and their clinical presentations overlap with many similarities (Beiselb, 1996). In resource-limited settings where laboratory diagnosis of malaria and HIV is not always possible, it would be useful to have a clinical algorithm that will raise the clinical suspicion of malaria and HIV infection in children with undernutrition. While some studies (Prazuck *et al.*, 1993; Ticklay *et al.*, 1997; Angami *et al.*, 2004; Bachou *et al.*, 2006) suggest that certain clinical features and co-morbidities may be more predictive of malaria and HIV infection in undernutrition, this has not been consistently demonstrated in the published literature (Kessler *et al.*, 2000). Clinical features reported as being predictive of malaria and HIV infection in children with undernutrition include lymphadenopathy, oral candidiasis, skin disorders, hepatomegaly, persistent diarrhoea, chronic discharging ears and prolonged fever. Clinical parameters that aid in the presumptive diagnosis of malaria and HIV in children have been summarized in the Integrated Management of Childhood Illness (IMCI) algorithm for suspected symptomatic malaria and HIV infection (WHO, 2008).

Studies suggest that between 8.6 and 54.0% of all children admitted to inpatient nutrition rehabilitation units in sub-Saharan Africa are malaria and HIV-infected (Amadi *et al.*, 2001; Madec *et al.*, 2011). No such comparable published data exist for DR. Congo. The current WHO guidelines (2015) recommend provider-initiated HIV testing and counselling (PITC) in clinical settings for all children in countries with an HIV prevalence of ⩾1% in the general population (Mutanga *et al.*, 2012; WHO, 2012). However, despite these recommendations, only 9.5% of inpatients (adults or children) were offered PITC in countries where the WHO PITC policy was adopted (Baggaley *et al.*, 2012). Early identification of malaria and

HIV infection will aid in reducing morbidity and mortality in both the children and their families.

The Sphere international standard project (2004) of less than 10% for therapeutic care has remained elusive for many of these. Moreover malaria, undernutrition and HIV are three of the most severe public health problems in Africa. The current study was conducted to determine the prevalence of malaria and HIV seropositivity among children with undernutrition admitted to the Kalembe-Lembe Pediatric Hospital. It also assessed the clinical predictors and outcome of malaria and HIV seropositivity in the study population.

Materials and methods

Study design, setting and participants

A cross-sectional, prospective study of children aged between 12 and 60 months, diagnosed with undernutrition, admitted to the Kalembe-Lembe Pediatric Hospital of Kinshasa was carried out between 10 July 2017 and 10 January 2018. Ethical approval was obtained from the Ministry of Health of DR. Congo and the ethical committee of China Tongji Medical College. Kalembe-Lembe is a Red Cross (Croix Rouge) hospital situated in Lingwala Municipality, Kinshasa City. It is the only referral hospital for the Kinshasa Metropolis in that it admits children with undernutrition aged between 12 months and 15 years. All children admitted to the hospital with HIV and with or without undernutrition, marasmus, kwashiorkor or undernutrition like defined according to weight-for-height *Z*-score (WHZ) <−3S.D. of the median WHO reference values (WHO, 2009) or with symmetrical oedema attributable to undernutrition (WHO, 1999) and as per the management protocol of the WHO (2011) were included in the study. Additionally, the included undernutrition participants' were diagnosed by calculation of the body mass index (BMI) combined with evaluation of brachial perimeter (PB). The children with undernutrition was classified as marasmus, kwashiorkor or oedematous undernutrition and classified as a marasmic-kwashiorkor (combination of both). The exclusion criterion in this study was the participants with a congenital haemoglobinopathies (sickle cell anaemia) and the refusal of parental consent or of the children consent. A sample size of 225 was calculated based on a prevalence of 17.4% reported by Fergusson *et al.* (2009) and a response rate of 90%. Recruitment was done prospectively until the sample size was reached. The recruitment process started with the agreement of the admission office staff; and after the attending medical team had completed their initial assessment and managed life-threatening complications. For all eligible children, the study was explained to the parent or guardian, and written informed consent was obtained. Parents/guardians of the patients were referred to the Voluntary Counselling and Testing centre to undergo pre- and post-test counselling.

Measurements and definitions

Blood was obtained by finger prick for thick smear malaria parasite test, and, HIV, while venous blood was collected into well-labelled ethylenediamine tetra acetate tubes for haemoglobin and haematocrit analyses. For those children who tested positive, their parents were also offered HIV testing. Testing for HIV was done by trained counsellors at the counselling unit of the hospital and consisted of two rapid HIV antibody tests (First Response and Ora Quick). Discordant results were retested with enzyme-linked immunosorbent assay (ELISA) and polymerase chain reaction (PCR).

The diagnosis of HIV disease was determined as follows: for HIV-1 DNA quantification, total HIV-1 DNA was extracted from 200 μL peripheral blood using Qiagen QIA symphony DNA Mini Kits (QIAGEN, Valencia, CA). The extraction of HIV-1 DNA and PCR for HIV-1 DNA was carried out using frozen samples. HIV-1 DNA in the peripheral blood [mainly white blood cells (WBCs)] was amplified and quantified for long terminal repeats gene using a fluorescence-based, real-time SUPBIO HIV Quantitative Detection Kit (SUPBIO, Guangzhou, China). The reaction system was as follows: reaction mixture 44.2 μL, enzyme 0.8 μL and DNA 5 μL. The housekeeping genes were amplified at the same time to quantify the cell amount. HIV-1 DNA were measured in duplicate and the quantification range of this assay was $20–5 \times 10^6$ of 8 copies per 10^6 WBCs. The amount of HIV-1 DNA per 10^6 peripheral blood mononuclear cells was calculated. All patients' with positives results underwent confirmatory tests by ELISA and PCR before being admitted in the hospital, according to the National Protocol of Management of HIV in DR. Congo. Four trained nutritionists and laboratory technicians assisted with the analysis and the anthropometric measurements. The relevant laboratory analyses, socio-demographic, anthropometric and clinical data were then recorded into a case report form. Data were collected specifically for the purposes of this study throughout admission until discharge by the principal investigator. The diagnosis of urinary tract infection was made only if it was culture proven. Severe anaemia was diagnosed if the haemoglobin level was $\leqslant 5$ g dL^{-1}. Malaria diagnosis was determined in concordance with WHO (2008, 2009). Uncomplicated (mild) malaria was defined by the seeking of treatment for symptoms consistent with malaria (i.e. fever, headache), axillary temperature >37.5 °C and parasite density <500 000 μL^{-1}. Severe (life threatening) malaria was defined as hyperparasitaemia ($\geqslant$500 000 μL^{-1}) or the presence of any parasite density associated with one or more of the following clinical criteria: cerebral malaria (Blantyre coma score $\leqslant$2, witnessed convulsions), severe anaemia (haematocrit level <15.0% or haemoglobin level <5 g L^{-1}), respiratory distress or prostration (inability to sit unassisted in a child usually able to do so) (Guindo *et al.*, 2007). The diagnosis of undernutrition was calculated by the BMI combined with evaluation of PB by the measured arm circumference, otherwise known as mid upper arm circumference (MUAC). Undernutrition was defined as BMI (kg m^{-2}) between 16.0 and 18.4, whereas when the BMI varied between 18.5 and 24.0 it was considered to be well-nourished (good nutritional status). Good nutritional status by MUAC was defined when the PB was $\geqslant$125 mm in children under 5 years of age, otherwise the child was considered to have undernutrition. In contrast, a PB $\geqslant$ 145 mm was a good nutritional status in children aged 5–9 years, while <145 mm of PB was estimated as undernutrition status. HIV seropositive children were referred to the Kalembe-Lembe Hospital HIV clinic for comprehensive management and follow-up. A confirmatory HIV antibody test was performed at 18 months in HIV exposed children and the results were documented. Anthropometric index variable was assessed by three different computational models: percentages from the median, percentile or *Z*-score.

Statistical analysis

Data were transported to Stata Intercool version 11.2 (StataCorp LP, 4905 Lakeway Drive, College Station, TX, USA) for analysis. Any variable with the substantial level of missing data was excluded from the analysis. Categorical variables such as sex and some clinical variables were analysed and presented as percentages with their 95% confidence intervals (CIs). Continuous variables were analysed and presented as means with standard deviation (S.D.) for normally distributed variables, and median with inter-quartile ranges (IQR) for skewed variables.

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Table 1. The prevalence of malaria and HIV according to selected risk factors

Malaria and HIV status *n* (%)				
Clinical variable	Positive *n*-168	Negative *n*-57	RR (90% CI)	*P* value
Fever	152 (84.3)	46 (73.6)	4.5 (2.8–7.6)	<0.001
Prolonged fever	59 (8.9)	33 (45.3)	5.8 (3.3–9.5)	<0.001
Diarrhoea	83 (46.6)	35 (48.2)	2.1 (1.8–2.5)	0.612
Prolonged diarrhoea*	66 (26.8)	32 (61.5)	4.5 (2.6–9.0)	<0.001
Cough	68 (38.6)	42 (58.2)	3.6 (3.2–9.2)	<0.001
Chronic cough*	57 (40.3)	41 (74.5)	9.0 (4.3–18.8)	<0.001
Poor Feeding	24 (74.9)	17 (35.1)	1.1 (1.0–1.3)	0.178
Vomiting	86 (58.2)	49 (42.5)	4.7 (3.3–8.4)	<0.001

*$P < 0.001$.

Table 2. Prevalence of malaria and HIV with other undernutrition complications and co-morbidities in the study population

Malaria and HIV status *n* (%)				
Clinical variable	Positive *n*-168	Negative *n*-57	RR (90% CI)	*P* value
Bacteraemia	52 (30.2)	32 (14.8)	1.5 (0.5–2.0)	0.145
UTI	22 (15.7)	18 (22.5)	1.2 (0.3–2.1)	0.291
Dehydration	78 (56.9)	46 (39.8)	8.7 (3.3–18.4)	<0.001
SA	86 (63.7)	40 (53.7)	7.5 (3.1–9.8)	<0.001
Pneumonia	25 (16.7)	12 (11.9)	2.3 (1.5–3.4)	0.657
PTB	88 (58.8)	45 (32.8)	8.5 (3.6–22.7)	<0.001

RR, risk ratio; CI, confidence interval; UTI, urinary tract infection; SA, severe anaemia; PTB, pulmonary tuberculosis.

Associations between various clinical variables of malaria and HIV status were determined and reported as risk ratios (RR), with the corresponding 95% CIs and *P* values, using Fisher's exact test. A stepwise logistic regression (Wald χ^2 statistic) was used to identify the most significant independent clinical predictors of malaria and HIV seropositivity. The diagnostic parameters (sensitivities, specificities, negative and positive predictive values) of the identified clinical predictors of malaria and HIV seropositivity were then determined. The clinical predictors were then combined in an algorithm to determine the likelihood of having malaria and HIV seropositivity based on the number of predictive clinical variables a child presents with. For all analysis, a two-sided *P* value $\leqslant 0.05$ was considered statistically significant.

Results

A total of 225 children were recruited in the current study and subdivided into five groups of 45 children including: the undernutrition, undernutrition + malaria, HIV + malaria + undernutrition, HIV + undernutrition groups and well-nourished group control. One-hundred and eleven (48.1%) children were males, median age was 40 (IQR: 36–48) months. In total, 140 were <30 months, 15 (7.3%) were orphans. Of the orphans, 10 (5.1%), 4 (1.8%) and 1 (0.5%) were maternal, paternal or had lost both parents, respectively. PITC was performed for all the patients with a test uptake of 100.0%. Among the 90 children aged less than 35 months or older in whom HIV antibody test was confirmed; only 37 (25.9%) that tested HIV seropositive were at high risk of dying. The age range for those in the malaria + HIV seropositive group was 12–60 months. Five of these presented with severe wasting and one had oedematous undernutrition.

Malaria and HIV seropositivity, anthropometric indices and clinical features

The mean WHZ for children ($n = 225$) was −5.5 (S.D. = 2.0). Significant differences occurred in undernutrition patients' groups with lower mean WHZ (−5.0 in comparison with −5.4 for undernourished children). Among malaria, HIV and undernourished group, 82.2% had severe wasting whereas among HIV and undernourished group, 17.9% had oedematous undernutrition. Of oedematous children with malaria and undernutrition, 40.1% had severe marasmic-kwashiorkor. The association between malaria and HIV seropositivity status, clinical features, co-morbidities and WHZ is shown in Tables 1 and 2. Malaria + HIV seropositivity were strongly associated with prolonged fever, cough and diarrhoea; oral thrush, generalized lymphadenopathy and pulmonary tuberculosis (PTB) (*P* value <0.001 for all parameters). In addition, malaria + HIV seropositivity was also significantly associated with cough, vomiting, lethargy or altered consciousness, skin rash and hepatomegaly (*P* value <0.05 for all parameters). However, severe anaemia was more likely in the malaria and HIV seropositive groups. The overall prevalence of haemoglobin was 6.8% and that of haematocrit was 10.2% in children with malaria and oedematous and HIV-positive undernutrition.

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Table 3. Predictors of malaria and HIV seropositivity in study population and their sensitivity and specificity

Clinical variable	Sensitivity% (90% CI)	Specificity% (90% CI)	PPV% (90% CI)	NPV% (90% CI)
Prolonged diarrhoea	26.8 (15.2–36.8)	95.3 (89.7–98.2)	65.3 (42.4–78.6)	85.6 (69.8–79.1)
Chronic cough	42.4 (30.3–55.1)	89.7 (92.2–93.5)	80.2 (60.6–90.1)	83.1 (78.2–88.2)
Prolonged fever	45.6 (35.4–59.1)	90.3 (88.6–93.6)	67.8 (58.6–85.6)	84.3 (77.3–86.2)
Sensitivities and specificities of a clinical algorithm consist of above variables.				
No of parameters identified	Sensitivity%	Specificity%	Correctly classified%	
⩾1	91.8	75.3	78.5	
⩾2	70.5	91.4	87.6	
⩾3	44.6	95.7	83.8	

CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.

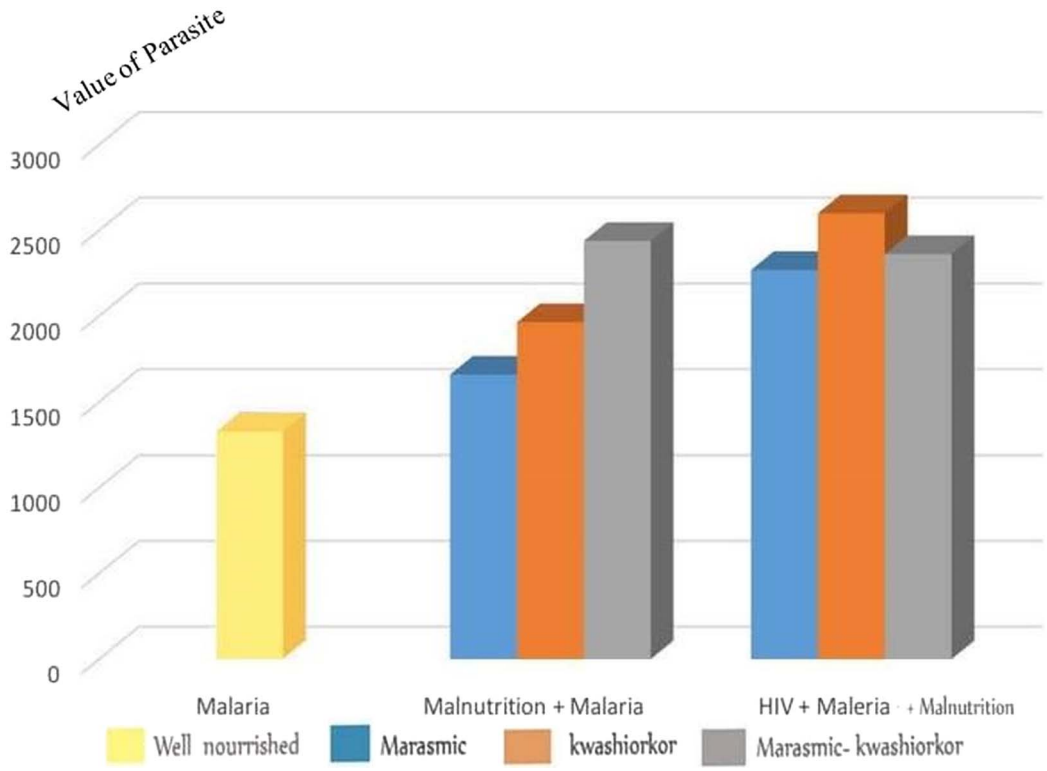

Fig. 1. Parasitaemia value *vs* various undernutrition group.

Development of a clinical algorithm

Table 3 shows the sensitivities and specificities of the strongest clinical predictors of malaria and HIV as independent variables and when grouped together in a clinical algorithm. The presence of three or more symptoms was highly specific for malaria and HIV seropositivity in the children, and could be used as presumptive diagnosis of malaria and HIV infection in children with undernutrition.

Survival and mortality rates

Malaria and HIV seropositive children had a significantly ($P < 0.001$) lower mean weight gain per kg per day (2.8, 90% CI = 0.8–4.2 g kg^{-1} day^{-1}) than malaria and HIV seronegative children (7.0, 90% CI = 6.7–7.8 g kg^{-1} day^{-1}). Two-hundred and three (83.4%) children survived while 22 (16.6%) died during admission. The mortality and weigh gain of the children was monitored during admission at hospital and at home. Malaria and HIV seropositive children had a significantly higher risk of dying (mortality rates in malaria and HIV seropositive children, 38.3%; P value <0.001). Eighteen (32.4%) out of the 22 malaria and HIV exposed children died during admission, one (2.9%) died at home after discharge. Overall, 11 (31.6%) children with malaria and HIV seropositive were lost follow-up at 18 months. However, 68% of them have been monitored as much as 47 months.

Parasitaemia

As shown in Fig. 1, increasing value of parasitaemia was directly proportional to undernutrition + malaria and undernutrition + malaria + HIV co infection; the parasite load gradually increased with the highest value of parasitaemia compared to controls and difference was statically significant ($P < 0.05$). However, comparison between haemoglobin and haematocrit variables with the HIV undernutrition group, malaria undernutrition group and HIV + malaria + undernutrition group is shown in Table 4. The value of haemoglobin and haematocrit gradually decreased for

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Table 4. Haemoglobin and haematocrit *vs* children with or without disease type

Gender/Hb Ht	Well nourished	Undernutrition	Undernutrition + malaria	Undernutrition + HIV	Undernutrition + malaria + HIV
F					
Hb	8.70 ± 2.12	7.58 ± 0.74	7.33 ± 0.59	6.87 ± 0.1	4.70 ± 0.96
Hct	24.37 ± 2.06	26.46 ± 1.72	22.35 ± 1.49	23.80 ± 1.81	22.47 ± 2.84
M					
Hb	9.10 ± 1.21	7.35 ± 0.76	7.30 ± 0.60	7.29 ± 1.25	5.17 ± 1.9
Hct	23.85 ± 3.28	26.38 ± 1.97	21.82 ± 1.43	24.95 ± 1.71	22.68 ± 2.75
Total					
HB	13.25 ± 1.66	7.46 ± 0.75	7.31 ± 0.59	7.08 ± 0.68	4.94 ± 1.43
Ht	24.11 ± 2.67	26.42 ± 1.84	22.09 ± 1,46	24.38 ± 1.76	22.58 ± 2.78

Hb, haemoglobin; Hct, haematocrit.

the undernutrition group, undernutrition + malaria group, undernutrition + HIV group, HIV group and undernutrition + HIV group compared to controls with significant difference for the haemoglobin variable ($P < 0.003$).

Discussion

Our results showed 0.1% prevalence of HIV (including participants with HIV alone and malaria/HIV co-infection) in DR. Congo. This observation was consistent with the reported prevalence of HIV by Médecins Sans Frontières (2015), as well as for the prevalence (median, 0.2%) in the Joint United Nations Program on HIV and AIDS (UNAIDS) global report of 2014 and 2015. However, the current results were inconsistent when compared to other reports (Sanyaolu *et al.*, 2013). This study found a PITC uptake of 100% which could be attributed to the 'opt out' approach utilized, and the skills of the trained counsellors at Kalembe-Lembe.

Malaria and associated HIV infection accounted for 29.2% in this study, which is low when compared to that of 17 African countries with an overall prevalence reported in a meta-analysis study by Fergusson *et al.* (2009). The interaction between malaria and HIV prevalence could be explained as established in previous report by Certad *et al.* (2003) who suggested that lower CD4+ T cells are related to increased risk of parasitic infections. Among malaria and HIV seronegative children with undernutrition, the mortality rate was almost that of the minimum by international standard, of ⩽10.0% (Fergusson *et al.*, 2009). Moreover, additional reports have shown that the interaction between of malaria and HIV potentiated the increase in mortality rate when compared to malaria and HIV seronegative children more especially with associated undernutrition (Amadi *et al.*, 2001; Guindo *et al.*, 2007; Sanyaolu *et al.*, 2013; Kenyon and Buyze, 2015) and concomitant lower rate of weight gain. This could be due to the higher prevalence of potentially life-threatening co-morbidities such as PTB, bacteraemia and diarrhoeal diseases, which correlates with HIV. It could also be related to the fact that malaria and HIV-infected children are more likely to have complicated case management issues such as multiple pathology, drug–drug interactions and drug toxicities. While Fergusson *et al.* (2009) found no significant difference in the rate of weight gain by malaria and HIV status, though a higher mortality in malaria and HIV seropositive group was observed. Thus, in view of the poorer prognosis in malaria and HIV seropositive children with undernutrition we consider that there should be well developed linkages between malaria and HIV clinics.

Anthropometric and clinical variables in HIV-positive children with malaria and HIV were more likely to be classified under severe wasting than oedematous undernutrition, which was consistent with the findings of other authors (Kessler *et al.*, 2000; Amadi *et al.*, 2001; WHO, 2008). Children enrolled in this study included those with marasmus, kwashiorkor and marasmic-kwashiorkor, with malaria and HIV and other chronic diseases such as PTB. Traditionally, marasmus has been reported in children ⩽60 months of age (Idemyor, 2007). The results of the current study also showed a higher median parasite density in HIV-positive as wells as undernutrition + HIV positive groups than that in well-nourished groups of malaria, which was relatively opposite to the finding of previous studies in Nigeria (Sanyaolu *et al.*, 2013). However, the haematocrit and haemoglobin were lower in all groups compared to the malarial group. This may be explained by the fact of the synergy between of undernutrition + HIV in causing immune suppression. Malaria susceptibility between HIV-infected undernutrition and well-nourished children may relate to the timing of acquisition of age-dependent immunity. Nutritional differences between HIV-infected associated undernutrition and HIV-infected in well-nourished children could influence susceptibility to malaria, including micronutrient deficiencies. However, more detailed characterization of nutritional status in these children is lacking, therefore it is difficult to comment on the identified potential factors that could alter these infection risks. Previous studies have reported that individuals with HIV are considered to be at high risk of malaria in endemic areas (Leaver *et al.*, 1990; Atzori *et al.*, 1993; Niyongabo *et al.*, 1994; Idemyor, 2007; Sanyaolu *et al.*, 2013). A similar phenomenon was observed in our data, because the DR. Congo is considered an endemic area.

Survival has improved dramatically; however, challenges still remain. In a country like the DR. Congo with a relatively high malaria and HIV prevalence, health workers may not have a high enough index of suspicion of malaria and HIV co-infection to request PITC under appropriate settings. Therefore, there is limitation in the management of HIV. Thus, there is need to determine the RR and correlation between malaria and HIV. Our results showed high prevalence of malaria and HIV, which was higher in the following co-morbidities and conditions: pneumonia, tuberculosis and dehydration. This may be linked to the underlying weakening of the immune system which increases the susceptibility to these infections.

Furthermore, the predictors of malaria and HIV seropositivity in the study population and their sensitivity and specificity revealed a strong association between HIV, malaria and chronic: diarrhoea, cough and fever.

Limitations of the study

Some limitations of this study include its cross-sectional nature as well as the small sample size of participants co-infected with malaria and HIV that was analysed. Whether the cause of the

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undernutrition was primary was not determined; although the secondary causes of undernutrition that were detected were documented. The different diets received by the children were also another possible limitation of this study. Additionally, the study period fairly covered the two major seasons in the DR. Congo; it may not have been truly representative of children admitted to Kalembe-Lembe Pediatric Hospital throughout the year.

Conclusion

The prevalence of HIV and malaria in our study was higher than expected (29.2%). HIV infection was significantly associated with malaria and undernutrition as well as other morbidities. The results indicate that malaria and HIV infections are a major public health risk to undernourished children. When malaria is associated with co-morbidities such as HIV and undernutrition, there is gradual increase in parasitic density and gradual decrease in haemoglobin and haematocrit.

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Conflict of interest. None.

Ethical standards. This work was carried out with the approval of the ethical committee of China Tongji Medical College and the Ministry of Health of DR. Congo.

References

Amadi B, Kelly P and Mwiya M (2001) Intestinal and systemic infection, HIV, and mortality in Zambian children with persistent diarrhea and undernutrition. *Journal of Pediatric Gastroenterology and Nutrition* **32**, 550–554.

Angami K, Reddy SV and Singh KI (2004) Prevalence of HIV infection and AIDS symptomatology in undernourished children a hospital-based study. *Journal of Communicable Diseases* **6**, 45–52.

Atzori C, Bruno A and Chichino G (1993) HIV-1 and parasitic infections in rural Tanzania. *Annals of Tropical Medicine and Parasitology* **87**, 585–593.

Bachou H, Tylleskär T and Downing R (2006) Severe undernutrition with and without HIV-1 infection in hospitalised children in Kampala, Uganda: differences in clinical features, haematological findings and CD4+ cell counts. *Nutrition Journal* **5**, 27.

Baggaley R, Hensen B and Ajose O (2012) From caution to urgency: the evolution of HIV testing and counselling in Africa. *Bulletin of the World Health Organization* **90**, 652–658.

Beiselb WR (1996) Nutrition and immune function: overview. *Journal of Nutrition* **126**, 2611S–2615S.

Certad G, Arenas-Pinto A and Pocaterra L (2003) Isosporiasis in Venezuelan adults infected with human immunodeficiency virus: clinical characterization. *The American Journal of Tropical Medicine and Hygiene* **69**, 217–222.

Fergusson P, Chinkhumba J and Grijalva-Eternod C (2009) Nutritional recovery in HIV-infected and HIV uninfected children with severe acute undernutrition. *Archives of Disease in Childhood* **94**, 512–516.

Guindo A, Fairhurst RM and Doumbo OK (2007) X-linked G6PD deficiency protects hemizygous males but not heterozygous females against severe malaria. *PLoS Medicine* **4**, e66.

Idemyor V (2007) Human immunodeficiency virus (HIV) and malaria interaction in sub-Saharan Africa: the collision of two titans. *HIV Clinical Trials* **8**, 246–253.

Kenyon CR and Buyze J (2015) No association between gender inequality and peak HIV prevalence in developing countries – an ecological study. *AIDS Care* **27**, 150–159.

Kessler L, Daley H and Malenga G (2000) The impact of the human immunodeficiency virus type 1 on the management of severe undernutrition in Malawi. *Annals of Tropical Paediatrics* **20**, 50–56.

Leaver RJ, Haile Z and Watters DA (1990) HIV and cerebral malaria. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **84**, 201.

Madec Y, Germanaud D and Moya-Alvarez V (2011) HIV prevalence and impact on renutrition in children hospitalised for severe undernutrition in Niger: an argument for more systematic screening. *PLoS ONE* **6**, e22787.

Mutanga JN, Raymond J and Towle MS (2012) Institutionalizing provider-initiated HIV testing and counselling for children: an observational case study from Zambia. *PLoS ONE* **7**, e29656.

Niyongabo T, Deloron P and Aubry P (1994) Prognostic indicators in adult cerebral malaria: a study in Burundi, an area of high prevalence of HIV infection. *Acta Tropica* **56**, 299–305.

Prazuck T, Tall F and Nacro B (1993) HIV infection and severe undernutrition: a clinical and epidemiological study in Burkina Faso. *AIDS (London, England)* **7**, 103–108.

Sanyaolu AO, Fagbenro-Beyioku AF and Oyibo WA (2013) Malaria and HIV co-infection and their effect on haemoglobin levels from three healthcare institutions in Lagos, southwest Nigeria. *African Health Sciences* **13**, 295–300.

The SPHERE Project (2004) *Humanitarian Charter and minimum Standards in Disaster Response*, 2nd Edn. Minimum standards in food security, nutrition and food aid. Switzerland, Geneva: The Sphere Project, pp. 103–202.

Ticklay IM, Nathoo KJ and Siziya S (1997) HIV infection in undernourished children in Harare, Zimbabwe. *East African Medical Journal* **74**, 217–220.

WHO (1999) *Management of Severe Undernutrition: A Manual for Physicians and Other Senior Health Workers*. Geneva, Switzerland: WHO.

WHO (2007) *WHO case Definitions of HIV for Surveillance and Revised Clinical Staging and Immunological Classification of HIV-Related Disease in Adults and Children*. Geneva, Switzerland: WHO.

WHO (2012) Service Delivery Approaches to HIV Testing and Counselling (HTC): A Strategic HCT Programme Framework. https://apps.who.int/iris/handle/10665/75206

WHO, UNAIDS, Unicef (2011) Global HIV/AIDS Response. Epidemic update and health progress towards universal access. Progress Report.

WHO, Unicef (2008) *Integrated Management of Childhood Illness for High HIV Setting*. Geneva, Switzerland: Chart Booklet.

WHO, UNICEF (2009) WHO child growth standards and the identification of severe acute undernutrition in infants and children. A Joint statement by WHO and UNICEF.

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