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Features associated with underlying HIV infection in severe acute childhood malnutrition: a cross sectional study

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**Abstract**

Introduction

Up to half of all children presenting to Nutrition Rehabilitation Units (NRUs) in Malawi with severe acute malnutrition (SAM) are infected with HIV. There are many similarities in the clinical presentation of SAM and HIV. It is important to identify HIV infected children, in order to improve case management. This study aims to identify features suggestive of HIV in children with SAM.

Methods

All 1024 children admitted to the Blantyre NRU between July 2006 and March 2007 had demographic, anthropometric and clinical characteristics documented on admission. HIV status was known for 904 children, with 445 (43%) seropositive and 459 (45%) seronegative. Features associated with HIV were determined.

Results

Associations were found for the following signs: chronic ear discharge (OR 14.6, 95%CI 5.8-36.7), lymphadenopathy (6.4, 3.5-11.7), clubbing (4.9, 2.6-9.4), marasmus (4.9, 3.5-6.8), hepatosplenomegaly (3.2, 1.8-5.6), and oral Candida (2.4, 1.8-3.27). Any one of these signs was present in 74% of the HIV seropositive, and 38% of HIV uninfected children. A history of recurrent respiratory infection (OR 9.6, 4.8-18.6), persistent fever, recent outpatient attendance, or hospital admission were also associated with HIV. Persistent diarrhoea was no more frequent in HIV (OR 1.1). Orphaning (OR 2.1,1.4-3.3) or a household contact with TB (OR 1.7,1.1-2.6), were more common in HIV. Each of these features were present in > 10% of seropositive children. HIV infected children were more stunted, wasted, and anaemic than uninfected children.

Conclusions

Features commonly associated with HIV were often present in uninfected children with SAM, and HIV could neither be diagnosed, nor excluded using these. We recommend HIV testing be offered to all children with SAM where HIV is prevalent.

Introduction

90% of childhood HIV occurs in Africa, and is associated with 7% of all deaths in children aged under 5 (1). Severe acute malnutrition (SAM) is a common presentation of HIV(2) in Malawi, with up to half of children admitted to nutrition rehabilitation units INRUs se.cohesive, for HIV

In a metaanalysis of African studies on SAM, overall mortality in HIV infected children was 30.4%, compared with 8.4% in HIV negatives (4). HIV infected children may have different care needs during admission(5), and community interventions such as cotrimoxazole (6) and ARVs (7)-can reduce their long term mortality. Parental diagnosis and treatment may also be relevant, reducing orphaning and improving child survival (8). To access these services HIV infection needs first to be identified.

There are many similarities in the clinical presentations of SAM and HIV. This is partly due to a cell mediated immunodeficiency in SAM, (9, 10), but also due to malnutrition arising from poor appetite and a catabolic state in advanced HIV (11). A cycle of infection, malnutrition and immunodeficiency has been described (12). Once within this cycle, many of the clinical manifestations are similar. Previous studies have attempted to identify which clinical features are suggestive of underlying HIV infection in malnutrition (13), with adenopathy, oral Candida and marasmus being most sensitive. The child's parental health and past medical history have not been evaluated previously.

Some of the clinical features recognized in SAM, such as oral Candida, are staging criteria for HIV(14) or markers of HIV in presumptive diagnosis of infants(14), including malnutrition itself. Nutritional features which may help identify underlying HIV in a child with SAM include wasting (marasmus), reported to be 4.6 times more common in HIV infection (3.13.15-20), and a weight <60% of the expected median for age (18).

Oral candidiasis is more common in HIV (2, 13, 21-24), though not in all studies in malnutrition (18). Chronic suppressive otitis media (CSOM) has been reported as more common in HIV infection, both on pediatric wards (2), and in the NRU (24).

Diarrhea is common in children presenting with SAM, with enteropathy and persistent diarrhea (PD) common in HIV (21, 25), though intestinal helminths appear equally prevalent(26,27). Clubbing, indicative of chronic lung disease (CLD) is seen in HIV (2), though not specifically reported in SAM. Lymphadenopathy (13, 24) has been associated with HIV in children presenting with SAM. Anemia occurs more commonly, with a mean hemoglobin of 8.3g/dl in HIV, compared to 8.8g/dl in uninfected children with SAM (28).

The aim of this study is to describe the clinical, and demographic associations of SAM with, and without, underlying HIV. These features could play a role in identifying children with HIV, so the diagnosis of HIV can be confirmed, and children directed to specific HIV pathways as early as possible.

Methods

All children admitted to the Queen Elizabeth Central Hospital NRU, Blantyre, Malawi, between July 2006 and March 2007 were included in the study. It was nested within a randomized trial on improved foods for SAM(29). As part of the trial, all
children were assessed in detail at admission. Admission criteria were: Weight for Height (WH) <70% of median NCHS reference, a Mid Upper Arm Circumference (MUAC) < 110mm, or the presence of bilateral non-pitting oedema (kwashiorkor). Children were weighed on Tanita 1582 digital scales, and length and MUAC were measured to the nearest 1mm using locally made height boards and MUAC tapes (UNICEF). 

HIV counseling and testing (HCT) was offered for all children, usually after initial stabilization. This involved two ELIS A rapid tests (Determine® and Uni-GoldTM), with a third (Hema StripTM or SD-Bioline®) for discordant results.

PCR was unavailable for definitive diagnosis in children <18 months of age, and CD4% available only exceptionally. A waiting list for ARVs at the time of admission was a wider distribution of ages in the HIV infected children, one month older than in the uninfected. There was limited laboratory analysis available for comparison, as only packed cell volume (PCV) and malaria films were routinely available. PCV was 30.4% in HIV uninfected. A household contact with TB was more common (14.4% v.s. 8.9%), as was a past history TB treatment in the child.

Family history 
Maternal orphaning was reported in 11% of HIV seropositive children, and loss of a father in 9.9%, double the rates in the HIV uninfected. A household contact with TB was more common (14.4% v.s. 8.9%), as was a past history TB treatment in the child.

Clinical signs and symptoms according to HIV status are shown in table 1, presented by strength of association. HIV was most strongly associated with chronic suppurative otitis media (CSOM) with an odds ratio (OR) of 14.6 (95%CI 5.8-36.7). Lymphadenopathy (OR 6.4, 95%CI 3.5-11.7), clubbing (4.93, 2.63-9.4), marasmus (4.8, 3.53-6.83), hepato-splenomegaly (3.2, 1.8-5.6), and oral Candida (2.4, 1.8-3.27) had the next strongest associations. Any one of these signs was present in 74% of the HIV seropositive, though 38% of HIV infected children also presented with one of these. More than half the children with HIV presented with kwashiorkor.

Malnutrition was more severe in HIV infected children (tables 2 and 3), who were more underweight for age (mean Z score difference [AZJ 0.49], more wasted (AZ 0.73), and had more severe stunting (AZ 0.84). Significantly more were underweight, with 79% below the third percentile weight for age, compared to 53% of uninfected children. Only children infected with HIV had Kaposis sarcoma (4), or Herpes Zoster (1), and 13 of the 15 children with parotid swelling were HIV seropositive.
Although marasmus is strongly associated with HIV, previous reports had implied that oedematous malnutrition was uncommon in HIV. The majority (54%) of children with HIV in this study presented with oedema, consistent with reports of oedema in 67% and 71% from Malawi (6, 18) and Uganda at 37-43% (13, 21, 34). Many studies have found persistent diarrhoea to be much more common in paediatric HIV (2, 25, 33) with a relative risk of 6.1 reported on the wards in Blantyre (2). However we found similar levels in children with SAM, present in 21% in HIV uninfected children and 23% of those with HIV. Others have similarly reported no differences in diarrhoea prevalence in SAM (13, 18, 21, 24).

Anthropometry

Although marasmus is strongly associated with HIV, previous reports had implied that oedematous malnutrition was uncommon in HIV. The majority (54%) of children with HIV in this study presented with oedema, consistent with reports of oedema in 67% and 71% from Malawi (6, 18) and 50% in Zambia (17), though rates were lower in Burkina Faso and Uganda at 37-43% (13, 21, 34).

Children with HIV were significantly more wasted, stunted and underweight, with twice the proportion of uninfected children being < -4 standard deviation (Z) scores for each of these parameters. This reflects the chronic nature of HIV, with larger nutritional deficits in the HIV infected. Modification of the standard treatment guidelines for SAM may be appropriate, and knowledge of HIV status is therefore important (5). Children recover less quickly with HIV (35), and weight gain is associated with degree of immunodeficiency (19).

Clinical signs predictive of HIV

We found CSOM to have the strongest association with HIV. This has been reported as more common in SAM in Zimbabwe (24), and noted in to be associated with HIV (2) on the paediatric wards in Malawi. Recurrent respiratory infections are a staging criteria in HIV (14), so it might be expected that previous ill health and more frequent medical attendance, would also be associated with HIV.

Lymphadenopathy was the sign most strongly associated with HIV in SAM in Burkino Faso (13) with sensitivity of 25% and specificity of 96%, a similar finding to that in Zimbabwe (24). Clubbing indicative of chronic lung disease, has been reported as and predictive of HIV (2), though not reported in SAM. Prazuck reported a strong association with hepatomegally (13), though Kessler (18) in Malawi found no difference in prevalence of this. Although we identified a significant association with oral Candida, this occurred in over 20% of uninfected children, making it an unreliable marker of HIV infection in SAM. Candida is commonly cited as associated with HIV (2, 13, 22-24).

Many studies have found persistent diarrhoea to be much more common in paediatric HIV (2, 25, 33) with a relative risk of 6.1 reported on the wards in Blantyre (2). However we found similar levels in children with SAM, present in 21% in HIV uninfected children and 23% of those with HIV. Others have similarly reported no differences in diarrhoea prevalence in SAM (13, 18, 21, 24).

Breastfeeding

For children under 2 years of age, there was a 3 fold greater risk of being HIV seropositive if still breastfed. Although this could reflect reduced maternal to child transmission of HIV with early cessation of breastfeeding (36), most mothers were unaware of their HIV status. A more likely explanation is that HIV uninfected children rarely present whilst breastfeeding, as breast milk is an excellent source of nutrition, and protects against diarrhoeal and respiratory infections. Weaning the child off the breast is commonly associated with the development of SAM. Kessler (18) in Blantyre found a similar association with breastfeeding in HIV, although did not disaggregated for age under 2 years. In Zimbabwean children under 15 months no significant association with breastfeeding was found (24).

Orphaning

Orphaning has been reported to be associated with poorer outcomes in children born to mothers with HIV, irrespective of their HIV status (8). This has only been reported in one study on malnutrition, and was no more frequent in HIV (24), possibly as orphaning has a large impact on survival of all children, as it impacts on food security and care. We found children with HIV twice as likely to have lost either mother or father, however this had also occurred in 8.8% of the HIV uninfected.

Laboratory

Anaemia was more severe, with a small but significantly lower PCV observed in the HIV infected. This corresponds to a difference of 0.3g/dl haemoglobin, similar to the 0.6g/dl reduction previously noted in Malawi (28), but greater than that in Uganda (21). This does not appear to be due to malaria, which occurred less frequently n the HIV infected.

Conclusion

We have identified those clinical features strongly associated with HIV in severe malnutrition. These signs may allow some children with HIV to be better recognized when admitted to the ward. However in this study many of these features occurred in SAM not related to HIV.

The common distinguishing features in HIV infected children being < -4 standard deviation (Z) scores for each of these parameters. This reflects the chronic nature of HIV, with larger nutritional deficits in the HIV infected. Modification of the standard treatment guidelines for SAM may be appropriate, and knowledge of HIV status is therefore important (5). Children recover less quickly with HIV (35), and weight gain is associated with degree of immunodeficiency (19).
children without malnutrition include persistent diarrhoea and oral candidiasis, both of which are frequently observed in SAM. In severe malnutrition CSOM, lymphadenopathy, clubbing, and hepatosplenomegaly were found to be of greatest predictive of HIV, as was the presence of severe stunting or wasting. A child still breastfeeding, orphaned, or with a history of recent admission or clinic attendance, is also suggestive of HIV infection, as is a history of TB in the family. Most of these features had Odds Ratios >2 and a prevalence in the HIV infected child over 10%, making them sufficiently common to be of use in assessing patients for features of HIV.

These features had significant overlap in SAM and HIV, and many severely malnourished children with HIV have none of these features present. In view of this we would recommend offering HCT to all children admitted with SAM in HIV prevalent environments. In our experience, this approach was acceptable to families. The ability to link families to HIV services is critical to high HCT uptake, as it can be explained to the family that there are specific, life prolonging treatments available, making knowledge of HIV status beneficial to both child and family.

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References

Features associated with underlying HIV infection


