

The College of Medicine is often host to students from abroad. Lisa Kessler came from USA and stayed longer than most - a full year as a Fulbright Scholar attached to the Department of Paediatrics. She took a very active role as an advocate for improved nutritional supplies to the Nutritional Rehabilitation Units in the Southern and Central Districts. This paper is the result of a research project that she initiated.

The impact of HIV infection on the clinical presentation of severe malnutrition in children at QECH

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Abstract

A study was undertaken in a central nutritional rehabilitation unit (NRU) in southern Malawi to assess the impact of HIV infection on clinical presentation and case fatality rate. The HIV seroprevalence for 250 severely malnourished children over 1 year of age was 34.4% and the overall mortality was 28%. HIV infection was significantly more associated with marasmus (62.2%) than with kwashiorkor (21.7%) [$p < 0.0001$]. Clinical and radiological features were not helpful in distinguishing HIV infected from non HIV infected children. The in-hospital case fatality rate was significantly higher for HIV infected children (38.4%) compared to severely malnourished children without HIV infection (22.7%) [$p < 0.05$]. Though HIV infection contributes to the high mortality experienced in NRU's in Malawi, we argue that more remediable contributing factors still need to be addressed.

Introduction

Severe malnutrition is common in Malawi and is a leading cause of childhood mortality along with malaria and pneumonia (1). Oedematous malnutrition (kwashiorkor and marasmic-kwashiorkor) consistently accounts for around 75% of the admissions to nutritional rehabilitation units (NRUs) in southern Malawi with a case fatality rate of 20-30% (2). Unfortunately, this in-hospital mortality rate is similar to other low income countries in Africa (3,4) though is much higher than acceptable.

This high mortality is associated with late presentation of severe disease; overcrowded and under-resourced wards; unreliable supplies of food; and a lack of important micronutrients such as zinc or potassium. Human immunodeficiency virus (HIV) infection is now likely to be an important additional factor contributing to both the incidence of severe malnutrition and the high mortality. Due to high vertical transmission rates, there has been a marked increase of childhood HIV infection over the last decade (5). Paediatric HIV infection often presents with recurrent infection and failure to thrive leading to severe malnutrition. The aim of this study was to assess the impact of HIV infection on the clinical

presentation and in-hospital mortality of severely malnourished children admitted for nutritional rehabilitation.

Methods

A study was undertaken in Moyo House, the nutritional rehabilitation unit at Queen Elizabeth Central Hospital in Blantyre. The majority of children present from the urban or peri-urban areas of Blantyre district either as a primary presentation or as a referral from peripheral NRUs. Referrals from peripheral urban and rural NRUs were common at the time of the study because nutritional support to those units had been reduced over the previous two years. The study was undertaken over a two month period during the rainy season (January 15th until March 15th), which is the peak time of year for both malnutrition admissions and mortality.

Clinical data were collected on a standard admission sheet, by two paediatricians (HD, GM). Progress was monitored using a standardised critical care pathway with the help of a specially designated audit nurse. Malnutrition was defined using the Wellcome classification i.e. marasmus: below 60% weight-for-age; marasmic/kwashiorkor: below 60% weight-for-age plus oedema; kwashiorkor: above 60% weight-for-age plus oedema. Hepatomegaly was defined as a liver palpable more than two centimetres below the costal margin at the mid clavicular line. Axillary lymphadenopathy was the presence of axillary nodes larger than 0.5 centimetres in size.

The paediatrician was unaware of the HIV status of the child. Treatment is per standard protocol. Children with oedematous malnutrition receive a low energy, low protein diet (70 kcal energy/kg/day, 1.2g protein/kg/day) for the initial phase until there is symptomatic improvement of diarrhoea, irritability and appetite, usually 5 to 7 days. They are then changed to a high energy, high protein diet (170 kcal energy/kg/day; 5.8g protein/kg/day) for rapid catch-up growth. Children with marasmus are usually started on the high energy, high protein diet unless there is severe diarrhoea.

All children receive multivitamin supplementation but not iron supplementation. All children are prescribed oral cotrimoxazole on admission for one week, though will receive parenteral antibiotics (chloramphenicol +/- gentamycin) if considered to have clinical sepsis at any stage.

Nasogastric tube feeding is uncommon and not well accepted. The large numbers of admissions with overcrowding and the risk of nosocomial infection, along with the lack of nursing staff and nutritional supplies requires that children are discharged once they are considered recovered from the acute illness. For marasmus with good appetite, this often meant discharging early with supply of food for the mother/guardian to feed at home. Such supplies are no longer available. For oedematous malnutrition, this usually means discharging after resolution of oedema and an improvement in mental state and appetite. The number of deaths that occur after discharge is not known, though must be considerable.

Consent was obtained from the parent/guardian for inclusion in

the study. The first 150 children included in the study were offered a routine chest x-ray (CXR). Following this, a CXR was done only for a specific clinical reason due to cost restraint. It was explained that HIV serostatus would be performed anonymously by a paediatric laboratory technician after the clinical study was completed and that the results would not be available to them during the hospital stay. However, those that wished to know their child's HIV status or, in instances where the clinician suggested testing, the usual hospital procedure including pre-test counselling was undertaken with a sample sent to the main hospital laboratory. No mother or guardian refused either HIV testing or routine chest radiograph. HIV antibody testing was for HIV-1 and HIV-2 (HIV SPOT, Genelabs Diagnostics, Singapore) on one sample only. All children admitted to the paediatric wards routinely have a finger-prick sample taken for a thick film for malaria parasites and a packed cell volume (PCV). CXR films were examined by a panel including the hospital radiologist and paediatricians unaware of the clinical data or HIV status of the child.

Data analysis used a computer statistics programme (Epi Info 6). Only seropositive and seronegative children over a year of age were compared. The association between variables was determined using Yates corrected Chi-square test. The study was approved by the College of Medicine Research Committee.

Results

282 children were enrolled in the study over the two month period. 15 were excluded from analysis due to unsuccessful blood sampling and 7 were excluded due to loss of the clinical file after discharge. 143 were male and 117 were female. The mean age of children was 2.18 years age (range 6 months to 10 years). Children with oedematous malnutrition were significantly older than marasmus children. The mean age for kwashiorkor and marasmus-kwashiorkor was 2.24 and 2.33 respectively, compared to 1.73 for marasmus. 25% (57/226) of mothers were separated from the father of the child and 92% (209/228) were up to date with immunisations, according to their road-to-health card.

The overall HIV seroprevalence was 35% (n=260). The prevalence for children over 12 months of age was 34.4% (n=250). The ten infants will not be included in further analysis as HIV antibody positive is not considered diagnostic of infection under 1 year of age.

Table 1. Clinical type of malnutrition and HIV prevalence

	Number	HIV Positive (%Prevalence)	
Kwashiorkor	106	23	(21.7%)
Marasmic-Kwashiorkor	99	35	(35.4%)
Marasmus	45	28	(62.2%)
Total	250	86	(34.4%)

Table 1 reports the frequency of the clinical form of malnutrition and its relationship to HIV seropositivity, with a significantly higher seroprevalence among marasmic children compared to children with oedematous malnutrition ($X^2=17.35$, p value, 0.0001).

Table 2. Clinical presentation and outcome in relation to HIV seropositivity in children over 1 year.

	HIV Positive	HIV Negative n=86 (%)	p value n=164 (%)
History			
Still breast fed	30 (34.9)	22 (13.4)	<0.0001
Diarrhoea	66 (76.7)	109 (66.5)	NS
Fever	48 (55.8)	82 (50.0)	NS
Cough	45 (52.3)	70 (42.7)	NS
Anorexia	63 (73.3)	95 (57.9)	<0.05
Irritability/Apathy	73(84.9)	111 (67.7)	<0.05
TB contact	18 (20.9)	32 (19.5)	NS
Examination			
<60% wt-for age	62 (72.1)	84 (51.2)	0.001
Oral thrush	21 (24.4)	24 (14.6)	NS
Axillary lymphadenopathy	20 (23.2)	29 (17.9)	NS
Hepatomegaly	28 (32.6)	67 (40.9)	NS
Skin ulcers	14 (16.3)	34 (20.7)	NS
Splenomegaly	7 (8.1)	20 (12.2)	NS
Anaemia (PCV<18%)	12 (13.9)	12 (7.3)	NS
Outcome			
On TB treatment	13 (12.4)	19 (20.1)	NS
Mean time to resolution of Oedema (days)	9.6 days	9.7 days	NS
Case fatality rate	33 (38.4)	37 (22.7)	<0.05

Table 2 outlines the comparison of clinical presentation and outcome between HIV positive and HIV negative children with severe malnutrition.

A history of anorexia or behaviour changes. The overall in-hospital mortality was 28%, significantly higher for HIV seropositive children than for seronegative children (38.4% v 22.7%; p value <0.05).

A chest radiograph was performed in 148 children. Twenty nine or 56.9% of 51 HIV reactive children were considered to have an abnormal CXR compared to 52 or 53.6% of 97 HIV non-reactive children. The commonest abnormality was diffuse bilateral infiltration and the pattern of abnormalities did not differ between the two groups.

Discussion

The overall seroprevalence among severely malnourished children over 12 months of age admitted for nutritional rehabilitation was found to be 34.4%. As this study was undertaken during the peak malnutrition season, the relative

contribution of HIV is likely to be even greater during the dry season. This compares to an earlier survey from Moyo house of 519 malnourished children conducted in 1993 which found a seroprevalence of 15.4% (unpublished data, Dr S. Legget). Similar studies from Africa have found HIV-seroprevalence ranging from 14% in Rwanda in 1989 and Burkina Faso in 1989/90 to 48.6% in Zimbabwe in 1993/94 (6-8), reflecting an increase in prevalence and burden of childhood HIV infection. In neighbouring Zambia in 1990/91, a seroprevalence of 41% was found among children admitted for malnutrition in Lusaka compared to 28% overall seroprevalence for paediatric admissions (9).

Marasmus is associated with HIV infection more than kwashiorkor, also consistent with these earlier studies from the region. Severe wasting is a recognised feature of paediatric AIDS. Kwashiorkor is not strongly associated with HIV infection, except when it occurs with wasting (marasmus-kwashiorkor) or in a breast-fed child as previously observed by Brewster *et al* (2). A recent report from Cote d'Ivoire also found a significantly higher HIV seroprevalence of 50.9% with marasmus compared to 20% with kwashiorkor (10). Marasmus tends to be associated with more chronic disease of earlier onset as occurs with HIV infection, whereas kwashiorkor tends to have a more acute onset in often less stunted and better nourished children, typically precipitated by the cessation of breast feeding (11).

HIV infection does add a considerable burden to the number of malnourished children presenting for nutritional support. Aside from the presence of wasting and a history of still being breast fed at the time of admission, we found few objective findings on presentation that distinguished the HIV infected malnourished child. Though behaviour changes such as irritability and apathy were significantly more common, they are characteristic of children with kwashiorkor. Other studies have shown significant associations with generalised lymphadenopathy and oral thrush (7,8). No study has yet demonstrated clinical features of sufficient specificity and sensitivity to be of great assistance to the clinician.

The pattern of chest radiograph (CXR) abnormalities was very similar between the HIV infected and non-HIV infected groups. Pulmonary tuberculosis (PTB) is another cause of malnutrition, though is difficult to prove in young children. The diagnosis is often considered on the basis of a close household contact, usually a parent. However, the strong epidemiological link between PTB and HIV in young Malawian adults puts the child contact at risk for both diseases. CXR abnormalities found with HIV infection, with pulmonary TB and for malnutrition are often non-specific (11, 12).

We found significantly higher case-fatality among the HIV positive malnourished children. Thus, HIV infection seems to make a significant contribution to the consistently high case-fatality rate that occurs in our malnutrition unit. We would also expect that it contributes to mortality after discharge. Kurawige

et al found a 75% mortality among HIV-1 seropositive malnourished children at 2 year follow-up compared to 23% among seronegative children. The average time between hospitalisation and death was 5.7 months (6).

Sepsis is a common cause of death in malnourished children and co-infection with HIV is likely to increase the risk of sepsis. In a brief report, Wilkinson *et al* in South Africa demonstrated a reduction in mortality from 20% to 6% using prophylactic parenteral antibiotics on all admissions and improved nursing care including prompt treatment for hypoglycaemia (13). Seasonal influences were not considered in the analysis and clinical data was not provided. Such an approach in our setting would require greater resources that are currently available.

At the time of this study, the WFP had withdrawn its support for many of the NRU's, though this policy has since been reviewed. The NRU's in Malawi have for many years been supplied with milk powder from overseas and locally produced maize-soy mix, oil, sugar and beans by the WFP through the Ministry of Health. Micronutrients, such as zinc or potassium, are not available in Malawi and have generally only been attained with specific funding. Recent research conducted within our unit has demonstrated the superiority of milk over maize-based diets and the importance of micronutrients in reducing mortality (2,14,15). A questionnaire circulated to all NRU's in Malawi in 1996 found that only 4 of 25 units had all the recommended food items available at the of the survey. It was also reported that the number of feeds being given per day ranged from 2 to 10, with 11 units giving less than 6 feeds per day (16). It is clear that major improvements are still required in the areas of supply and supervision.

An important aim of audit is to inform for more effective management. Given the decreasing support of nutritional supplies, the overcrowded wards during the rainy season, and the likely poor long-term outcome, it might be suggested that HIV infected malnourished children would be best managed at home. That such an approach is often taken is suggested by the low percentage of marasmic children being admitted to the unit. Many marasmic children are seen on our general wards and outpatient clinics who do not get admitted to the NRU. Offering less active management to HIV infected individuals always poses an ethical dilemma. Infected children are not easily identifiable clinically and routine HIV testing may result in mothers receiving information that may be more damaging than helpful (17).

Kwashiorkor is usually not a result of HIV infection. The frustration that surrounds the failure to improve the management of kwashiorkor over the years in our setting remains. The move towards community-based projects aimed at prevention are sensible and important, but until these efforts bear fruit, nutritional rehabilitation units will continue to be overburdened with acute malnutrition requiring therapeutic feeding i.e. nutritional supplies and adequate nursing staff.

Acknowledgements

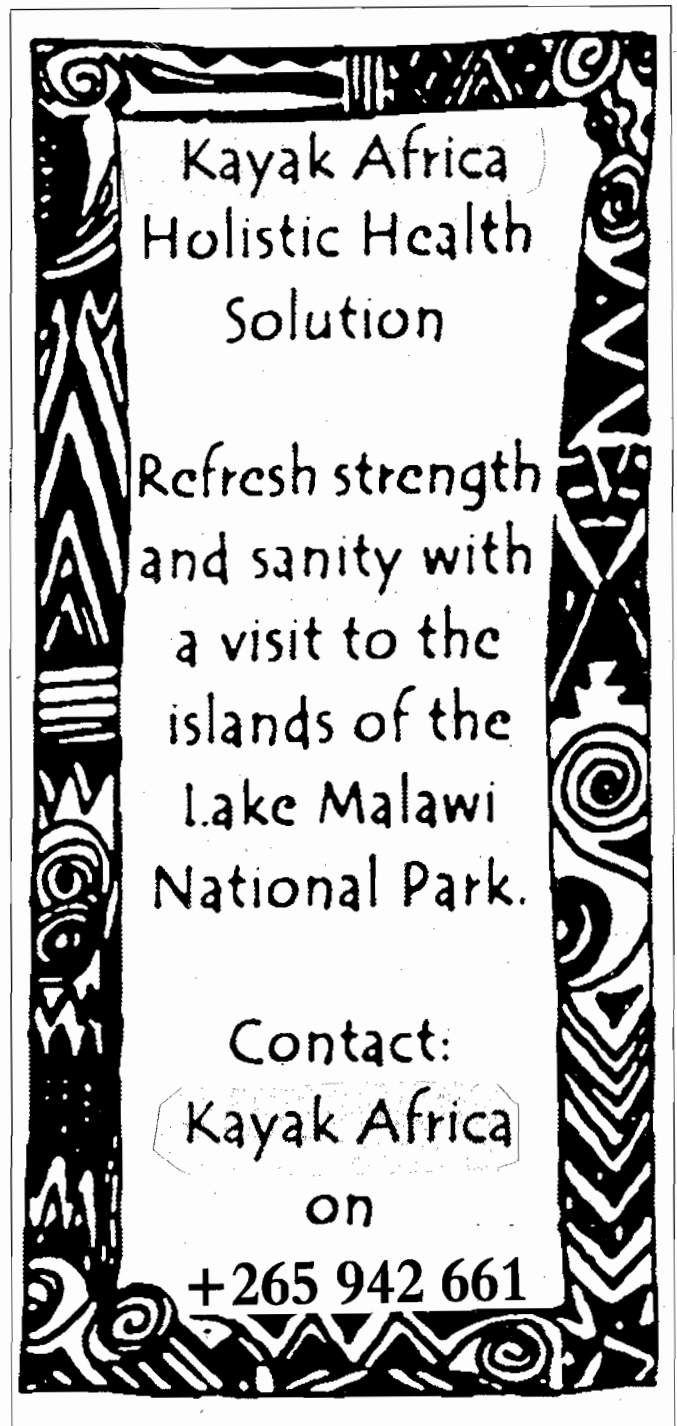
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References

1. Anonymous. Malawi Demographic and Health Survey, 1992. Malawi Government, Zomba, 1994.
 2. Brewster DR, Manary MJ, Graham SM. Case management of kwashiorkor: an intervention project at seven nutrition rehabilitation centres in Malawi. *European Journal of Clinical Nutrition* 1997;51:139-147.
- Brewster DR, Greenwood BM (1993) Seasonal variation of paediatric diseases in the Gambia, West Africa. *Annals of Tropical Paediatrics* 13:133-146.
- Gamatie Y, Prual A, Wollo J, Huguet D. Are paediatric wards in developing countries only places to die? A study of prior to hospitalisation risk factors of death among 0-2 year old hospitalised children in Niamey, capital of Niger. *Journal of Tropical Paediatrics* 1994;40:54-57.
- Coulter JBS. HIV infection in African children. *Annals of Tropical Paediatrics* 1993;13:205-215.
- Kurawige J-B, Gatsinzi T, Kleinfeldt V, Rehle T, Bulterys M. HIV-1 infection among malnourished children in Butare, Rwanda. *Journal of Tropical Paediatrics* 1993;39:93-95.
- Prazuck T, Tall F, Nacro B, et al. HIV infection and severe malnutrition: a clinical and epidemiological study in Burkina Faso. *AIDS* 1993;7:103-108.
- Ticklay IMH, Nathoo KJ, Siziya S, Brady JP. HIV infection in malnourished children in Harare, Zimbabwe. *East African Medical Journal* 1997;74:217-220.
- Chintu C, Luo C, Bhat G, et al. Impact of the Human Immunodeficiency Virus type-1 on common paediatric illness in Zambia. *Journal of Tropical Paediatrics* 1995;41:348-353.
- Beau JP, Imboua-Coulibaly L. Kwashiorkor and HIV: new questions. *Journal of Tropical Paediatrics* 1997;43:50-51.
- Waterlow J. Protein Energy Malnutrition, Edward Arnold, London, 1992.
- Schaaf HS, Beyers N, Gie RP et al. Respiratory tuberculosis in childhood: the diagnostic value of clinical features and special investigations. *Pediatric Infectious Disease Journal* 1995;14:189-194.
- Wilkinson D, Scrase M, Boyd N. Reduction in in-hospital mortality of children with malnutrition. *Journal of Tropical Paediatrics* 1996;42:114-115.
- Brewster DR, Manary MJ, Menzies IS, Henry RL, O'Loughlin EV. Comparison of milk and maize based diets in kwashiorkor. *Arch Dis Child* 1997;76:242-248.
- Brewster DR, Manary MJ. Potassium supplementation in kwashiorkor. *Journal of Paediatrics Gastroenterology and Nutrition* 1997;24:194-201.
- Grabosch E. Assessment of the nutritional situation in NRU's of Malawi. October to November 1996. *Malawi Medical Journal* 1998; 11:11-14.
- Temmerman M, Ndinya-Achola J, Ambani J, Piot P. The right not to know HIV test results. *Lancet* 1995;345:969-970



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