Summary

Background: Severe acute malnutrition (SAM) is a worldwide problem although it commonly occurs in children living in low-income countries. SAM may be associated with reduced relative contribution of whole-blood polyunsaturated fatty acids (PUFA) yet PUFA play very important roles in the body such as immune modulation, growth and development as well as maintenance of skin water barrier among others. The reduced relative contribution of PUFA may be linked to some of the clinical presentations in children with SAM. Children with complicated SAM require in-patient management during which complications are treated as well as initiation of therapeutic feeding. Before the current study we were aware that despite following a well defined protocol of management of SAM, it was not always successful. We did not know whether the treatment offered was able to correct all deficiencies that were present in the malnourished children – particularly restoring PUFA status which had not received much attention. And we also did not know whether our rehabilitation would permit an optimal catch up, both in terms of growth and development and intellectual function - for which PUFA may be crucial. Furthermore, little attention has been given to the effects of feeds on the PUFA status of children with SAM in the recovery period. One of the strategies during nutritional rehabilitation is to encourage physical activity as soon as the child is well enough. Subjective methods have been used to measure physical activity while objective measures have not been widely used to quantify physical activity in children recovering from SAM. There is need to evaluate the PUFA status of children admitted with complicated SAM and to assess changes of these PUFA during recovery as well as measure the level of physical activity. Treatment of SAM may be improved by better understanding of most of the nutritional deficiencies with the aim of achieving optimal nutritional status.

The purpose of this thesis was to investigate whole blood PUFA composition and its correlates in children admitted with SAM and describe changes in the PUFA composition in these children during treatment and to determine predictors of change. Furthermore, to assess the level and predictors of physical activity at discharge among these children.

Methods: The papers in this thesis are based on the FeedSAM study, a clinical cohort among 120 children aged 6 to 59 months, admitted for in-patient treatment of SAM at Mwanamugimu Nutrition Unit, Mulago National Referral Hospital, Kampala, Uganda, between October 2012 and June 2013. Background characteristics, dietary history i.e. breastfeeding and fish intake and information about

symptoms were collected by interviews with caretakers. Clinical examination and anthropometric measurements were done on admission and venous blood samples take for haemoglobin, C-reactive protein and fatty acid measurement. Vital signs and feeding were monitored daily during hospital admission. In paper I, we presented whole blood fatty acid composition at admission and correlated it with clinical data such as oedema, levels of haemoglobin, C-reactive protein and HIV-infection status. Clinical data and fatty acid composition were also obtained in 29 well-nourished healthy control children. In paper II, we investigated changes in whole-blood PUFA during transition, at discharge, eight and 16 weeks of follow-up. We further determined predictors of changes in the PUFA values during recovery from SAM. In paper III, we presented physical activity level and identified its predictors at discharge from hospital.

Results: The relative contribution of saturated fatty acids in whole blood were lower in 108 children with SAM compared to 24 well-nourished controls whereas most monounsaturated fatty acids were higher in children with SAM. All n-6 PUFA as well as total n-3 PUFA and docosahexaenoic acid (22:6n-3, DHA) were lower in children with SAM. The n-6: n-3 PUFA ratio was also lower in the children with SAM. Haemoglobin was a positive correlate of arachidonic acid (20:4n-6, AA), n-3 docosapentaenoic acid (22:5n-3, n-3 DPA), DHA, total n-6 LCPUFA and total n-3 LCPUFA. HIV infected children had less n-6 LCPUFA and AA than the un-infected children.

Whole blood n-6 PUFA proportions increased from admission to follow up, except for AA, which decreased from admission through transition to discharge. n-3 LCPUFA decreased through the entire period of treatment and follow-up. This decrease was greater in children from families with recent fish intake and those with naso-gastric tube feeding.

At discharge, the children had a mean (SD) physical activity of 285 (126) counts per minute (cpm). Weight-for- height z-score on admission, mid-upper arm circumference at discharge and whole-blood DHA on admission were positive predictors of physical activity, whereas duration of stabilization phase and hospitalization were negative predictors.

Conclusion: Children with SAM present to hospital with lower proportions of LCPUFA than the controls. HIV infection and low haemoglobin are associated with lower proportions of LCPUFA,

which may be related to lower numbers of blood cells. Despite advances in the management of SAM, current therapeutic feeds do not correct whole-blood LCPUFA composition, particularly n-3 LCPUFA, in children with SAM. The level of physical activity at discharge among children with SAM is very low perhaps indicating inadequate recovery from SAM. These results point to the fact that nutrition rehabilitation interventions need to increase the intake of PUFA especially n-3 LCPUFA. The results also suggest that assessment of physical activity may be used as a marker of recovery.