Chronic disease outcomes after severe acute malnutrition in Malawian children (ChroSAM): a cohort study

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Summary

Background Tackling severe acute malnutrition (SAM) is a global health priority. Heightened risk of non-communicable diseases (NCD) in children exposed to SAM at around 2 years of age is plausible in view of previously described consequences of other early nutritional insults. By applying developmental origins of health and disease (DOHaD) theory to this group, we aimed to explore the long-term effects of SAM.

Methods We followed up 352 Malawian children (median age 9·3 years) who were still alive following SAM inpatient treatment between July 12, 2006, and March 7, 2007, (median age 24 months) and compared them with 217 sibling controls and 184 age-and-sex matched community controls. Our outcomes of interest were anthropometry, body composition, lung function, physical capacity (hand grip, step test, and physical activity), and blood markers of NCD risk. For comparisons of all outcomes, we used multivariable linear regression, adjusted for age, sex, HIV status, and socioeconomic status. We also adjusted for puberty in the body composition regression model.

Findings Compared with controls, children who had survived SAM had lower height-for-age *Z* scores (adjusted difference *vs* community controls 0·4, 95% CI 0·6 to 0·2, p=0·001; adjusted difference *vs* sibling controls 0·2, 0·0 to 0·4, p=0·04), although they showed evidence of catch-up growth. These children also had shorter leg length (adjusted difference *vs* community controls 2·0 cm, 1·0 to 3·0, p<0·0001; adjusted difference *vs* sibling controls 1·4 cm, 0·5 to 2·3, p=0·002), smaller mid-upper arm circumference (adjusted difference *vs* community controls 5·6 mm, 1·9 to 9·4, p=0·001; adjusted difference *vs* sibling controls 5·7 mm, 2·3 to 9·1, p=0·02), calf circumference (adjusted difference *vs* community controls 0·49 cm, 0·1 to 0·9, p=0·01; adjusted difference *vs* sibling controls 0·62 cm, 0·2 to 1·0, p=0·001), and hip circumference (adjusted difference *vs* community controls 1·56 cm, 0·5 to 2·7, p=0·01; adjusted difference *vs* sibling controls 1·83 cm, 0·8 to 2·8, p<0·0001), and less lean mass (adjusted difference *vs* community controls –24·5, –43 to –5·5, p=0·01; adjusted difference *vs* sibling controls –11·5, –29 to –6, p=0·19) than did either sibling or community controls. Survivors of SAM had functional deficits consisting of weaker hand grip (adjusted difference *vs* community controls –1·7 kg, 95% CI –2·4 to –0·9, p<0·0001; adjusted difference *vs* sibling controls 1·01 kg, 0·3 to 1·7, p=0·005,)) and fewer minutes completed of an exercise test (sibling odds ratio [OR] 1·59, 95% CI 1·0 to 2·5, p=0·04; community OR 1·59, 95% CI 1·0 to 2·5, p=0·05). We did not detect significant differences between cases and controls in terms of lung function, lipid profile, glucose tolerance, glycated haemoglobin A_{1c}, salivary cortisol, sitting height, and head circumference.

Interpretation Our results suggest that SAM has long-term adverse effects. Survivors show patterns of so-called thrifty growth, which is associated with future cardiovascular and metabolic disease. The evidence of catch-up growth and largely preserved cardiometabolic and pulmonary functions suggest the potential for near-full rehabilitation. Future follow-up should try to establish the effects of puberty and later dietary or social transitions on these parameters, as well as explore how best to optimise recovery and quality of life for survivors.

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Introduction

Tackling severe acute malnutrition (SAM) is a major global health priority, as emphasised by its inclusion in the Sustainable Development Goals (SDGs).[1] Although SAM-related mortality has been well described,[2] little is known about its long-term effects on the health or quality of life of survivors. As global child mortality falls, these long-term considerations are becoming increasingly important. Generation Nutrition, a recent major campaign, emphasises this need to look at the long-term health effects of SAM.[3] For programmes and policies to effectively achieve such goals, further evidence is needed.

One potential long-term outcome for individuals who survive SAM is an increased risk of non-communicable diseases (NCDs) in later life.[4,5] Extensive evidence has linked variability in early life nutrition with adult health and NCDs:[6] a topic referred to as developmental origins of health and diseases (DOHaD). Most evidence for DOHaD describes associations between in utero or very early postnatal exposures and adult NCD risk. However,

Research in context

Evidence before this study

Very few studies have investigated the long-term implications of severe acute malnutrition (SAM). In a 2012 literature review, Bahwere and colleagues searched PubMed and Google Scholar using the terms "protein energy malnutrition", "protein caloric malnutrition", "severe malnutrition", "marasmus", "kwashiorkor" and "after recovery", "post-discharge" or "long term". They found eight follow-up studies describing children between 6 and 18 months after discharge from SAM treatment. The major finding was persistent post-SAM stunting. Although some longer follow-up studies of SAM do exist, they used older case definitions of SAM, have small sample sizes, or focus only on survival and linear growth. By contrast, many studies have conducted long-term follow-up for low birthweight infants and identified an association between early life nutrition and adult health, especially non-communicable diseases (NCDs). This field of research is known as developmental origins of health and disease (DOHaD).

Added value of this study

Our study fills an important evidence gap that has emerged since treatment for SAM has improved and SAM-associated mortality has decreased: long-term consequences increasingly matter. Our data following up survivors of SAM 7 years after discharge from hospital covered a wide range of outcomes, as well as recruiting both sibling and community controls. The results help to define a potential further window of plasticity for DOHaD because they describe the effects of a nutritional insult during childhood rather than the fetal or early infant period.

Implications of all the evidence

We found that SAM has long-term implications for growth, body composition, and physical function 7 years after hospital discharge. Conversely, sitting height, head circumference, and cardiometabolic and pulmonary markers of NCD risk seem to be largely preserved. Combining evidence from this study with existing evidence for DOHaD suggests that survivors of SAM show traits of so-called thrifty growth. Further studies are needed to establish the full effects of SAM as these individuals undergo puberty and encounter other potential stressors such as increased access to diets high in fat and sugar during ongoing urbanisation of Malawi. Further research is also needed to enable public health programming and policy makers to reduce long-term consequences. It is no longer sufficient for children affected by SAM to just survive: interventions must also help them to thrive.

it is biologically plausible that the occurrence of an insult such as SAM during late infancy or early childhood could have similar lasting effects, since crucial growth and development occurs beyond infancy and even into puberty.[7] Both the physiological insult of an acute, extreme calorie shortage, and the rapid catch-up growth that occurs during and after treatment could have long-term implications. These early life events might contribute to the high burden of deaths caused by cardiovascular disease, diabetes, and lung disease in low-income and middle-income countries (which account for 80% of the 36 million deaths globally per year), necessitating the need for appropriate research.[8]

This study aimed to explore the long-term effects of SAM in children 7 years after they had been discharged from hospital where they were receiving treatment for SAM. We investigated the effects of SAM on growth, body composition, functional outcomes, and risk factors for NCDs in a large nutrition cohort in sub-Saharan Africa.

Methods

Study design and participants

The original prospective cohort consisted of 1024 patients admitted for treatment of SAM at the Moyo nutrition ward at Queen Elizabeth Central Hospital in Blantyre, Malawi, from July 12, 2006, to March 7, 2007. All patients were treated in accordance with the national guidelines at the time.[9] This treatment involved admission based on National Center for Health Statistics (NCHS) references and initial inpatient stabilisation for all children by use of therapeutic milk followed by nutritional rehabilitation at home with ready-to-use therapeutic food. Detailed baseline data were collected as part of the PRONUT study.[10] Median age at admission was 24 months (IQR 16–34). In a follow-up study at one year post-discharge (FuSAM),[11] 477 (47%) children from the original cohort remained alive; the surviving children from this study form the case group for the present follow-up, the ChroSAM study. For comparison, we aimed to recruit one sibling control and one community control per child in the case group. The sibling control was the sibling closest in age to the case child, limited to children aged between 4 and 15·9 years. The community control was defined as a child living in the same community, of the same sex, and aged within 12 months of the case child. We selected community controls randomly by spinning a bottle at the case child's home and enquiring door to door, starting from the nearest house to where the bottle pointed. Written informed consent was obtained from the children's parent or guardian. Any children who had ever been treated for SAM were not eligible as controls. Additional assent was sought from the child if they were older than 13 years. Ethical approval for the study was granted by the Malawi College of Medicine Research and Ethics Committee (reference P.02/13/1342), and the University College London Research Ethics Committee (reference 4683/001).