Association between severe acute malnutrition during childhood and variability in blood pressure during adulthood in low- and middle-income countries: the Lwiro Cohort Study in the Democratic Republic of the Congo

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ABSTRACT

Introduction: Little is known about the long-term outcomes of Severe Acute Malnutrition (SAM) during childhood. As such, this study aims to explore the association between childhood SAM and blood pressure (BP) variability in adulthood in a context without nutrition transition.

Methodology: We identified 524 adults (Median age: 22 years) who were treated for SAM during childhood in Eastern DRC between 1988 and 2007. They were compared with 407 community unexposed age-and-sex matched with no history of SAM. The variables examined for this study were the systolic (SBP), diastolic (DBP), mean (MBP) and pulse (PP) blood pressures, as well as high blood pressure (HBP) in adulthood. For comparison, linear and logistic regression models were used for analysing continuous and dichotomous variables, respectively.

Results: Of the 524 exposed located, 145 exposed were selected according to age. A total of 97 unexposed were recruited. Compared to unexposed, exposed had slightly higher SBP and PP after adjusting [SBP = 1.4 mm Hg (-2.2, 4.8) and PP = 2.6 mm Hg (-0.3, 6.0)]. However, their mean DBP was lower that of among the unexposed [-1.6 mm Hg (-4.6, 1.5)]. MBP and creatinine levels were comparable between the two groups. The prevalence of HBP adjusted for age was higher among exposed than unexposed (9.7% vs 5.3%). In addition, the odds of having HBP was higher among exposed than unexposed, however the difference was not statistically significant [ORa 1.9 (0.7, 5.6)]. Finally, using multiple regression, although the effect was not significant, SAM was a major contributor to HBP [OR 3.1 (0.9,10.9), p = 0.064], while being male and higher BMI were the only independent predictors among the young population of this study.

Conclusions: There was no significant impact from an episode of SAM during childhood on BP variability in young adults in a context without nutrition transition. However, people who experienced a period of SAM had a higher prevalence of HBP and a much higher risk of developing HBP than unexposed. Additional multicentre studies involving a larger cohort would provide greater understanding of the impact of SAM on the overall risk of BP disorders during adulthood.

Key-words: Long-term, childhood acute malnutrition, hypertension, follow-up, DR Congo

INTRODUCTION

Acute malnutrition (AM) is a major public health problem in low-income countries (LICs) (1). Every year, more than 5.9 million children under the age of five die worldwide and 45% of those deaths are attributed to malnutrition (2). There are currently 17 million children across the world suffering from severe acute malnutrition (SAM), of whom 27% live in Africa (1).

In the Democratic Republic of the Congo (DRC), food security has been severely compromised for decades. In the Eastern part of the country, in the province of South Kivu, 55% of the population face chronic food insecurity, aggravated by geopolitical instability linked to endemic armed conflicts which have been in a state of flux across the region since the 1990s (3). In this province, malnutrition has been endemic since the 1960s. One in two children under the age of 5 has chronic malnutrition (CM) and 3% have AM (4).

In parallel, like other LICs, the DRC is undergoing a phase of epidemiological transition, with the emergence of non-communicable chronic diseases (NCDs) in adults, such as obesity, type 2 diabetes mellitus and high blood pressure (HBP), while undernutrition still widely persists among children (5-10). According to the developmental origin theory for NCDs, there is a causal association between undernutrition during childhood and NCDs in adulthood (11).

A number of studies in high-middle income countries (HMICs) support the theory of "foetal programming of adult NCDs", initially proposed by Barker et al., in 1986 (12). This theory states that there is a link between foetal growth disorders and cardiovascular diseases (CVDs), HBP and metabolic syndrome in adulthood (13). This theory could explain part of the significant increase in cardiometabolic diseases in LICs (14). However, the episodes of undernutrition in childhood are also considered as promoting the development of certain NCDs in adulthood in HMICs (14-15).

Despite growing evidence on the negative long-term effects of childhood undernutrition observed in HMICs, there is surprisingly little data on the long-term outcomes of children treated for SAM in LICs (16-18).

Studies conducted in sub-Saharan Africa, in Uganda and Malawi showed that catch-up growth after an episode of SAM or delayed childhood growth, respectively, were associated with increased blood pressure (BP) in adolescence (18), and that pre-pubescent survivors of childhood SAM were at greater risk of subsequent NCDs, even though no clinical or biological

marker of these subsequent morbidities was identified seven years after nutritional rehabilitation (17). Conversely, subjects who remained emaciated throughout the monitoring period in Uganda had a lower BP compared to subjects who never experienced AM between childhood and adolescence (18).

Still in Africa, a study conducted in Nigeria showed a higher prevalence of HBP in participants born during the Nigerian Civil War (1968-1970), and who had been exposed to severe famine *in utero* and/or during childhood compared to unexposed subjects who lived in the same region before the war, in 1965-1967 (19).

In South Kivu, in the east of the DRC, a recent study identified an increased prevalence of HBP and obesity (20). However, the presumed role of childhood malnutrition in the increased burden of NCDs and related risk factors in the DRC has not been explored.

This was the reason for conducting this study, which aimed to assess the association between childhood SAM (before the age of five years) and the variability of BP in a cohort of young adults screened 11 to 30 years after nutritional rehabilitation, with no nutrition transition (environment with a monotonous, undiversified and low-quality food situation), living in the east of the DRC.

METHODOLOGY

a. Study area

The study was conducted at the "Centre de Recherche en Sciences Naturelles de Lwiro (CRSN-Lwiro)", in the health zones (HZ) of Katana and Miti-Murhesa in South Kivu, in the DRC. The Nutrition Department of this center has a pediatric hospital and four integrated health centers which monitor the health and nutrition of children in the community (21).

b. Population studied

The size of the sample was determined by the number of patients admitted for SAM to the Lwiro pediatric hospital (HPL) from 1988 to 2007 and living in Miti-Murhesa and Katana in 2018 (22). A total of 1,981 patients were treated for SAM during childhood at the HPL between 1988 and 2007. On admission to this hospital, the median age was 41 months and 70.8% of patients were aged between 6 and 59 months old (22). The nutrition diagnosis made at the time

[based on the weight-to-height ratio plotted on the local growth curve established by De Maeyer in 1959, the presence of nutritional edema, and serum albumin levels] (23) was reassessed using the ENA for SMART program, version October 2007, for standardisation according to the WHO child growth standards (24). Based on the WHO standards, only 84% of the children were classified as having SAM (22). The others, classified as having moderate acute malnutrition or not suffering from AM, were excluded from subsequent analyses. All of the children hospitalised were treated according to the guidelines at that time (23).

During the follow-up of these subjects who became adults in the meantime, ie. 11 to 30 years after nutritional rehabilitation, 524 subjects from the initial cohort who were still living in the HZs of Miti-Murhesa and Katana were surveyed (22). To assess long-term growth, these survivors (exposed) were compared to 407 unexposed randomly-selected from the community (22). Initially, we aimed to select one unexposed for each exposed. However, unexposed proved harder to recruit than exposed, as many feared the social stigma associated with childhood malnutrition. The selection of unexposed was also limited by the number of eligible adults in the community (22).

For this study, only subjects aged more than 25 years and who had been admitted for SAM before the age of five years were considered. According to these two criteria, 145 former malnutrition sufferers were selected (exposed group). A total of 97 individuals aged more than 25 years, out of the initial 407, were selected as unexposed. All the respondents provided signed informed consent for participation in the study, either by written signature or by fingerprints, depending on literacy.

c. Variables of interest

The main variables of interest were clinical markers for HBP during adulthood. HBP was defined as a systolic BP (SBP) $\geq$ 140 mm Hg and/or a diastolic BP (DBP) $\geq$ 90 mm Hg and/or the taking BP-lowering drugs. The mean BP (MBP) and pulse pressure (PP) were calculated using the following formulas: MBP = DBP + 1/3(SBP - DBP), and PP = SBP - DBP (24).

BMI (Body Mass Index) was calculated using the formula weight/height^2 (in kg/m^2) and BMI values were split into four categories: < 18.5 = underweight, 18.5 to 24.9 = normal, 25 to 29.9 = overweight and $\geq$ 30 = obese (25).

For HBP, the main exposure was a history of SAM during childhood. Other variables such as socio-economic status (assessed by occupational category), food diversity, sex and anthropometric measurements (BMI during adulthood) were taking into consideration when modelling for potential confounding factors.

The type and frequency of food consumption were evaluated using a food diversity score created by the World Food Programme (26,27). This score measures the dietary diversity of households, weighted according to frequency of consumption. We asked the head of the household (often the mother) how many days the household had eaten each of the ten following food groups in the last seven days: grains, tubers, legumes, vegetables, fruits, meat/fish, milk/dairy products, sugar, oil/fat, and condiments. The frequency with which each food group was consumed was then multiplied by its nutritional value, giving a score for each food group. Lastly, the scores for each food group were added to calculate the overall score. Depending on the total, a subject was considered as having an insufficient, borderline or satisfactory diet if his score was between 0–28; 28.5–42 and > 42 respectively (26,27). For salt consumption, each subject had to say whether they added dietary salt to food during meals. To measure the frequency of salt consumption, the participant chose one of the following responses: rarely, often or always.

Smoking was taken into account for subjects who reported being occasional or regular smokers (more than 3 days per week) of at least one cigarette (including hand-rolled cigarettes), pipe or other form of tobacco (28). Finally, we used the threshold of consuming at least 2 (women) or 3 (men) units of alcohol (beer or local alcoholic beverages, wines or spirits) per day, regularly (more than 3 times per week), for a subject to be recorded as a regular drinker of alcoholic beverages (29).

d. Data collection

Data were collected over a period of five months (August 2018-December 2018), and the collection took place in two steps, carried out by 20 trained community health workers (CHW) and 2 supervisors, assisted by local leaders, qualified nurses and community liaisons. The CHWs were the same as those who had helped identify the subjects during the gathering of the cohort (22).

The first step consisted of a home visit. During these visits, the CHWs administered a sociodemographic questionnaire translated into Kiswahili (language spoken in the east of the DRC) to the participants, took their anthropometric measurements and scheduled an appointment within 48 hours at the nearest hospital for the second step. This appointment involved taking a venous blood sample and BP measurements taken by properly trained nurses working in the various health facilities in the zone. Unlike the nurses and laboratory technicians who did not know whether a participant was an exposed or an unexposed, the CHWs knew this information.

The questionnaire covered variables relating to the participant's identity, their lifestyle (alcohol and tobacco consumption, dietary habits), their medical history, known cardiovascular risk (CVR) factors (family or personal) as well as their socio-economic status (education and occupation).

The anthropometric measurements considered were weight and height. Body weight was measured to the nearest 100 g, with the subject wearing only light clothing, using electronic scales (bathroom scales, Tanita Digital HD-325®). Height was determined using a SECA 206 cm® measuring device with the subject wearing no shoes, to the nearest 0.1 cm. The anthropometric measurements were taken according to WHO guidelines (30) and were quality controlled, meaning that they were taken independently by two members of the team. The final measurement was the average of the two measurements. In the event of a discrepancy of more than 300 g (weight) and/or 0.5 cm (height), a third measurement was taken. The average of the two closest measurements was then used.

For all participants, BP was measured at rest, the subjects having abstained from strenuous physical activity, tobacco and/or alcohol consumption and beverages with a stimulating effect such as coffee and tea for a period. BP was measured using an electronic device (OMRON Hem 7001E®, Tokyo, Japan). Three measurements were taken with the left arm held at heart level, at five-minute intervals, with the subject seated and relaxed for at least 5 minutes. The cuff size was adjusted to the size of each participant's arm. The average of the second and third BP measurements was used. If the SBP or DBP measurements differed by more than 10 mm Hg, a fourth measurement was taken and the mean of the two closest measurements was used.

Lastly, 4 ml of blood was drawn via antecubital venepuncture after 12 hours of fasting to determine serum creatinine levels using standard calorimetric enzymatic methods (CYAN smart CY009, Brussels, Belgium) at the laboratory of the general provincial referral hospital in Bukavu (tertiary hospital).

e. Statistical analysis

We used Stata version 13.1 software for all analyses. Categorical variables were summarised in the form of frequency and proportion. Quantitative data were presented as mean and standard deviation (SD).

The data from exposed and unexposed were compared using Chi-squared tests or Fisher's exact tests (for proportion) and with Student's t-tests (for means).

Linear and logistic regression models were used, respectively, for the continuous [creatinine levels and BP (systolic, diastolic, mean and pulse)] and dichotomous variables (HBP). The basic models only included the main exposure - SAM- providing an unadjusted difference in the means with a confidence interval of 95% (CI 95%) between exposed and unexposed for quantitative variables and an unadjusted odds ratio (OR) for HBP.

Different models were then constructed in order to analyse the effects of SAM after adjustment. The adjusted model included three nominal variables accounting for the fixed effects on BP of socio-economic status (based on occupational category), food diversity score and adult anthropometrics (BMI). The differences in the means and ORs are presented along with their CI 95%. In order to be included in the models, occupational category and food consumption were converted into dichotomous variables. For occupation and consumption, we considered subjects with a satisfactory food score and a management and administrative position for occupation as positive responses. Other categories were considered to be negative responses.

Conditions for applying a linear regression (normality, uniformity of variance and linearity) were verified via analysis of residuals, and goodness-of-fit was verified using the Hosmer and Lemeshow test.

RESULTS

We included a total of 145 subject exposed to SAM during childhood and 97 who were not as unexposed.

Table 1 shows the sociodemographic and economic characteristics of the study population.

The mean age and the ratio of men to women were similar for the two groups. Compared to unexposed, exposed had lower education level and lower skilled occupations. These differences were statistically significant. We did not however observe a significant difference in civil status, ethnic group, religious affiliation, or food and salt consumption between the two groups.

Tables 2 and 3 show the clinical and biological markers and the prevalence of the different risk factors for NCDs in the two groups.

Looking at NCD risk factors, none of the studied variable was significantly different between the two groups (Table 2).
Although overall low, HBP prevalence was clearly higher among exposed than among unexposed. Exposed had a mean PP higher than unexposed, while their DBP was lower than unexposed. However, the differences observed were not statistically significant. In addition, MBP, SBP and serum creatinine levels were similar between groups. However, the proportion of subjects with raised creatinine levels was significantly higher between unexposed than exposed (Table 3).

Table 4 shows the unadjusted and adjusted differences in HBP markers between the two groups.

The models show that after adjusting for BMI, food diversity score and socio-economic status, the differences in SBP, DBP and PP between exposed and unexposed increased, without reaching the threshold of statistical significance, while the difference between the MBP means decreased.

Table 5 shows a summary of the major independent predictors of HBP among the population.

After adjustment, the variables significantly associated with HBP were being male and having higher BMI. Exposure to SAM and a high socio-economic status were associated with a higher

risk of HBP, on the borderline of statistical significance. A satisfactory food diversity score was not associated with HBP.

DISCUSSION

Our aim was to analyse the potential association between an episode of SAM occurring before the age of 5 years and risk of raised BP in adulthood in an environment without nutrition transition.

Our results suggest that mean BP values measured were comparable between subjects who experienced SAM during childhood and those who did not. The prevalence of (known) HBP was almost twice as high in subjects who were exposed to SAM during childhood compared to control subjects. In addition, the risk of developing HBP during adulthood tended towards being three times higher among exposed than unexposed. This study indicates that being male and having a higher BMI were the main independent contributors to HBP among this still relatively young population.

To our knowledge, this study is the first from sub-Saharan Africa to assess the long-term effects of childhood SAM on BP variability in young adults after a monitoring period ranging from 11 to 30 years, after discharge from hospital, in a context of endemic malnutrition. Our study is original in several respects: it examined the variability of major contributors to BP, included subjects who continued to live in an unfavourable environment without nutrition transition, and its analysis considered several CVR factors including lifestyles (alcohol, tobacco and food diversity) and socio-economic status (with occupational category as a proxy).

As regards renal function, serum creatinine levels were comparable between the two groups. This lack of difference may result from the fact that kidney development mostly occurs during the intra-uterine period, with no new nephrons formed after birth (31). Therefore, contrary to what happens during intrauterine undernutrition, which leads to reduced numbers of nephrons in survivors, which may lead to long-term haemodynamic modifications and nephrocalcinosis, involved in the genesis of hypertension and chronic renal diseases in adulthood (31), our subjects likely had a satisfactory number of nephrons prior to SAM, that was stable and less sensitive to postnatal malnutrition. This would also partly explain the lack of difference in BP variability between the two groups. We did not observe any statistically significant difference between the two groups in terms of SBP, DBP, PP or MBP.

Our study shows that HBP prevalence was almost twice as high among those exposed to SAM than among unexposed. This result corroborates a study conducted in Nigeria that showed a higher prevalence of HBP in participants born during the Nigerian Civil War and who had been exposed to severe famine both *in utero* and during childhood, compared to control subjects who lived in the same region before th1965-1967 civil war (19).

The exposed presented an increased risk of developing HBP during adulthood, despite the difference observed being not being statistically significant, probably due to the small sample size of the study. The results of our work are consistent with those of a study conducted in Malawi on pre-pubescent children (17). This study in Malawi identified children exposed to SAM as not being at greater risk of developing HBP than children not exposed to SAM. Our results are also comparable to those of a study in rural Uganda which identified factors associated with recovery from undernutrition as being more significant with respect to the development of HBP during adolescence than undernutrition itself (18). In our study, the subjects lived in a context characterised by an absence of nutrition transition, with precarious socio-economic conditions persisting during and after recovery from SAM.

Nevertheless, our results differ from almost all studies conducted in HICs, which show that subjects with low birth weight and/or low weight gain in childhood were at statistically significant higher risk of developing HBP and/or having higher BP during adulthood than controls (32-34). This discrepancy may be caused by several factors, including different ethnicities, since our subjects were all sub-Saharan Africans whereas the vast majority of HICs inhabitants are Caucasians. These ethnicity-related differences could be attributed in part to genetic (35) and environmental factors. As such, sub-Saharan populations are characterised as having different determinants for the development of HBP and metabolic handling of normal or excess salt intakes, which could have a confounding effect on the data observed.

Secondly, there were major differences in age between the populations. The majority of our subjects were young adults (mean age 28 years), unlike those in studies from HICs (median age 50 years) (33,34,36,37). This would also partly explain the absence of effect of age on BP variability and the development of HBP, given that the effects of natural ageing on BP and HBP become more apparent after the age of 50 years (32). As our population was still relatively young, and given that the risk of NCDs increases with age, an additional 10-20 years of hindsight would be needed to likely increase HBP prevalence in this population.

Thirdly, lifestyle and socio-economic status before and after exposure to the episode of undernutrition differ between the two regions. In contrast to the studies conducted in HICs, our subjects spent their childhood in precarious nutritional conditions before experiencing one or more episodes of SAM, and then continued to live in an unfavourable environment in terms of food quality and security, without nutrition transition. In HICs, famines occurred in populations that generally had a high socio-economic status and good health prior to the episode of famine, and rapidly recovered this status afterwards (38-40), whereas our cohort remained relatively disadvantaged during and after the episode of SAM, and therefore unexposed to an obesogenic environment up to adulthood. As a rule, people in South Kivu have little access to processed and/or industrialised food. The population keeps on consuming local foods, with reduced fat content and poor in refined carbohydrates. However, one cannot rule out that target organs damage could become more apparent if they are subsequently exposed over long periods to Western-style lifestyles promoting weight gain.

The fourth reason could be the life history period of exposure to undernutrition. Our subjects were exposed to SAM during childhood and not *in utero*, as was the case in the majority of the HICs. In contrast to changes to organ structure and function during the intra-uterine period, which are only partially reversible (41), the majority of organs already reached full developmental maturity during the childhood, and the changes associated with SAM could be less permanent than those occurring during the rapid foetal growth period, reducing the long-term effects of childhood SAM compared with foetal malnutrition.

Lastly, the difference between the criteria for diagnosing undernutrition must be taken into consideration. In HICs, undernutrition was defined based on a reduction in weight gain whereas, in our population, undernutrition was defined on the basis of weight-to-height ratio, mid-upper arm circumference and/or the presence of nutritional edema. In addition, more than 90% of our subjects had delayed growth during childhood (22). Consequently, the effect of weight gain could be different in children who gained weight and height in a balanced way compared to those who gained weight and BMI, but had delayed growth. All of these factors may explain the differences in the findings observed.

We observed that only a higher BMI and being male were major independent predictors of HBP in adulthood among our population. Our results corroborate those of other studies (42,43). BP is known to increase alongside BMI. In addition, being male is a well-documented unmodifiable CVR factor (42-44).

There are clear limitations of this study. Firstly, there is the survival bias: only those subjects who survived to adulthood and were still present in the villages two decades after the episode of SAM were studied. There is, however, no obvious reason to consider that the association between nutritional state of children admitted for SAM and BP would be different among those lost to follow up, due to the fact the hospital admission characteristics did not differ between subjects lost to follow up and subjects included (22).

Secondly, our study sample was not very large. Certain differences might have reached statistical significance with a larger sample size.

Thirdly, we did not have data on birth weight and height, gestational age, and on whether individuals were born as twins, triplets, etc., or on rate of growth in the first years of life. These factors could be potential confounders as they are linked to both SAM and to unfavourable late-onset phenotypes in terms of NCDs (45).

Fourthly, there is uncertainty as to whether all of the unexposed recruited were in good health. Although they did not present with Kwashiorkor and were not treated for SAM, some of them may have presented with moderate malnutrition linked to unfavourable socio-economic conditions in the region, but not to the point of being admitted to a hospital. The constant unfavourable situation in which the two groups lived may substantively reduce any inter-group differences as regards certain CVR markers studied.

Finally, in our study, BP was only measured on one day, without subsequent control measurements. This could have altered the differences observed, in one direction or another.

CONCLUSION

Our results show that an episode of SAM in childhood has a weak impact on BP variability in young Congolese adults living in an environment without nutrition transition. However, subjects who experienced a period of SAM during childhood had a higher prevalence of HBP and a moderately higher risk of developing HBP than unexposed subjects. Multicentre studies involving larger cohorts of older adults would provide greater understanding of the impact of SAM on the overall risk of CVDs and BP disorders in adulthood. Finally, our results are sufficient to show that efforts to combat SAM and its consequences should remain a public health priority. Given the paradoxical of high prevalence of SAM in LICs and lack of scientific

data on the potential long-term consequences of SAM, our results provide useful insights in this field.

DECLARATIONS

Abbreviations

AM: Acute malnutrition
BMI: Body Mass Index
BP: Blood Pressure
CHW: Community Health Workers
CM: Chronic Malnutrition
CRSN-Lwiro : Centre de Recherche en Sciences Naturelles de Lwiro
CVDs: Cardiovascular Diseases
CVR: Cardiovascular Risk
DBP: Diastolic Blood Pressure
DRC: Democratic Republic of the Congo
HBP: High Blood Pressure
HMICs: High-Middle Income Countries
HPL: Lwiro Pediatric Hospital
HZ: Health Zones
LICs: Low-Income Countries
MBP: Mean Blood Pressure
NCDs: Non-Communicable chronic Diseases
OR: Odds Ratio
PP: Pulse Pression
SAM: Severe Acute Malnutrition
SBP: Systolic Blood Pressure
WHO: World Health Organization

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Availability of data and materials

All data generated or analyzed during this study are included in this published article [and its supplementary information files]

Contributors

PM, GB, DL and PD conceived and designed the experiments. PM and GN did the data collection. MD contributed to specific areas of the methods, data analysis, statistics, and quality control. PM analyzed the data and wrote the first draft of the manuscript with LdH. GB, GN, MD, JM, MH, DL, CJ, GQM and PD contributed to the writing of the manuscript and agree with the manuscript's results and conclusions. All authors have read the submitted manuscript.

Ethics approval and consent to participate

All the respondents provided signed informed consent for participation in the study, either by written signature or by fingerprints, depending on literacy. All procedures performed in this study were approved by the Institutional Ethics Committee of the Université Catholique de Bukavu and were in accordance with the 1964 Helsinki declaration and its later amendments.

Consent for publication
N/A

Competing interests

The authors declare that they have no competing interests.

REFERENCES

1. Goday, P.S. (2020). Malnutrition in children in ressource-limiter countries: Clinical assessment. In K.J Motil& A.G Hoppin (Eds.), Uptodate

2. Wang H, Bhutta ZA, Coates MM, Coggeshall M, Dandona L, Diallo K, et al. Global, regional, national, and selected subnational levels of stillbirths, neonatal, infant, and under-5 mortality, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. The Lancet. 8 oct 2016;388(10053):1725-74

3. Cirimwami JK, Ramananarivo S, Mutabazi AN, Muhigwa B, Bisimwa EB, Ramananarivo R, et al. Analyse de la situation de la sécurité alimentaire au sein des ménages du Sud-Kivu montagneux en République Démocratique du Congo. International Journal of Innovation and AppliedStudies 2019 05 ;26(2) :503-525

4. INS, Enquête par grappes à indicateurs multiples, 2017-2018, rapport de résultats de l'enquête. Kinshasa, République Démocratique du Congo.

5. UNICEF, WHO & GROUP WB. Levels and trends in child malnutrition. New York; 2017.

6. Ng M, Fleming T, Robinson M, Thomson B, Graetz N. Global, regional and national prevalence of overweight and obesity in children and adults 1980-2013: A systematic analysis. Lancet. 2014;384(9945):766-81.

7. Caleyachetty R, Thomas GN, Kengne AP, Echouffo-tcheugui JB, Schilsky S. The double burden of malnutrition among adolescents: analysis of data from the Global School-Based Student Health and Health Behavior in School-Aged Children surveys in 57 low- and middle-income countries. Am J Clin Nutr. 2018; 108:414-24.

8. Kimani-murage EW. Exploring the paradox: double burden of malnutrition in rural South Africa. Glob Health Action. 2013; 6:193-205.

9. Hanandita W, Tampubolon G. SSM -Population Health The double burden of malnutrition in Indonesia: Social determinants and geographical variations. SSM - Popul Heal. 2015; 1:16-25.

10. Wells JC, Sawaya AL, Wibaek R, Mwangome M, Poullas MS, Yajnik CS, et al. The double burden of malnutrition: aetiological pathways and consequences for health. Lancet. 2019;6736(19):1-14.

11. Barker DJP. Developmental origins of chronic disease. Public Health. mars 2012;126(3):185-9

12. Barker DJP, Osmond C. Infant mortality, childhood nutrition, and ischemic heart disease in England and Wales.The Lancet. 10 mai 1986;327(8489):1077-81

13. Barker D. The developmental origins of adult disease. J Am Coll Nutr. 2006;46(46):4-14

14. Victora CG, Adair L, Fall C, Hallal PC, Martorell R, Richter L, et al. Maternal and child undernutrition: consequences for adult health and human capital. Lancet. 2008;371(9609):340-57

15. Sawaya AL, Sesso R, Florencio TM, Fernandes MT MP. Association between chronic under nutrition and hypertension. Matern Child Nutr. 2005; 1:155–163.

16. Paluku Bahwere, Angella Mtimuni, Kate Sadler TB and SC. Long term mortality after community and facility-based treatment of severe acute malnutrition: Analysis of data. J Public Heal Epidemiol Vol. 2015;4(8):215-25.

17. Lelijveld N, Seal A, Wells JC, Kirkby J, Opondo C, Chimwezi E, et al. Chronic disease outcomes after severe acute malnutrition in Malawian children (ChroSAM): a cohort study. Lancet Glob Heal. 2016;4(9): e654-62.

18. Asiki Gershim, Robert Newton, Lena Marions, Anatoli Kamali and LS. The effect of childhood stunting and wasting on adolescent cardiovascular diseases risk and educational achievement in rural Uganda: a retrospective cohort study. Glob Health Action. 2019;12(1).

19. Hult M, Tornhammar P, Ueda P, Chima C, Bonamy AK, Ozumba B, Norman M. Hypertension, diabetes and overweight: looming legacies of the Biafran famine. PLoS One. 2010 ;5(10): e13582

20. Katchunga PB, Mirindi P, Baleke A, Twagirumukiza M. The trend in blood pressure and hypertension prevalence in the general population of South Kivu between 2012 and 2016: Results from two representative cross-sectional surveys — The Bukavu observational study. PLoS One. 2019; 05:1-14.

21. Action Contre la Faim. Enquête Nutritionnelle Anthropométrique dans la Zone de Santé de Miti-Murhesa,Province du Sud-Kivu,République Démocratique du Congo. 2011

22. Mwene-Batu P, Bisimwa G, Ngaboyeka G, Dramaix M, Macq J, Lemogoum D, et al. Follow-up of a historic cohort of children treated for severe acute malnutrition between 1988 and 2007 in Eastern Democratic Republic of Congo. PLOS ONE. 11 mars 2020;15(3): e0229675

23. Paluku B. Contribution à l'amelioration et à l'évaluation de la prise en charge globale de l'enfant hospitalisé en afrique centrale (Sud-Kivu). Université Libre de Bruxelles; 2002

24. Mancia G, Fagard R, Narkiewicz K, Redón J, Zanchetti A, Böhm M et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension. The Task Force for the Management of Arterial Hypertension

of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens. 2013; 31:1281-357

25. National Heart, Lung, and Blood Institute Obesity Education Initiative. The practical guide to identification, evaluation, and treatment of overweight and obesity in adults. Bethesda, MD: National Heart, Lung, and Blood Institute, 2000.

26. WPF, Calculation and use of the Food Consumption Score in food consumption and food security analysis, WFP Vulnerability Analysis and Mapping Branch, January 2008

27. IFPRI. Validation du score de consommation alimentaire du PAM par IFPRI [Internet]. 2014. Disponible sur: http://www.ifpri.org/sites/default/files/publications/ifpridp00870.pdf

28. Convention Cadre de l'OMS pour la lutte Antitabac. Recueil des indicateurs. Genève; 2015

29. Belgherbi S, Mutatayi C, Palle C. Les repères de consommation d'alcool : les standards mis en question. Obs français des Drog des Toxicom. 2015;1-160

30. WHO Multicentre Growth Reference Study Group: WHO Child Growth Standards: Length/ height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: Methods and development. Geneva: World Health Organization; 2006

31. A. Wilhem-Bals, H. Chehade, E. Girardin, E.Gonzalez PP. Immaturité rénale et oligonéphronie du prématuré : conséquences à long terme. Rev Med Suisse. 2014; 10:435-41

32. AlGhatrif M, Strait JB, Morrell CH, Canepa M, Wright J, Elango P, et al. Longitudinal trajectories of arterial stiffness and the role of blood pressure: the Baltimore Longitudinal Study of Aging. Hypertens Dallas Tex 1979. 2013 ;62(5) :934–41

33. Painter RC, Roseboom TJ, Bleker OP. Prenatal exposure to the Dutch famine and disease in later life: An overview. Vol. 20, Reproductive Toxicology. 2005. p. 345-52.

34. Roseboom TJ, van der Meulen JHP, Ravelli ACJ, Osmond C, Barker DJP, Bleker OP. Effects of prenatal expossure to the Ductch famine on adult disease in later life: an overview. Mol Cell Endocrinol. 2001;185(5):93-8.

35. Wells JCK. Ethnic variability in adiposity, thrifty phenotypes and cardiometabolic risk : addressing the full range of ethnicity , including those of mixed ethnicity. Obes Rev. 2012;13(Suppl.2):14-29

36. Ravelli ACJ, Van Der Meulen JHP, Osmond C, Barker DJP, Bleker OP. Obesity at the age of 50 y in men and women exposed to famine prenatally. Am J Clin Nutr. 1999;70(5):811-6

37. De Rooij SR, Painter RC, Roseboom TJ, Phillips DIW, Osmond C, Barker DJP, et al. Glucose tolerance at age 58 and the decline of glucose tolerance in comparison with age 50 in people prenatally exposed to the Dutch famine. Diabetologia. 2006;49(4):637-43

38. Burger, G. C. E., Sandstead, H. R., & Drummond JC. Malnutrition and starvation in Western Netherlands, September 1944 to July 1945: Part I and II.The Hague. Gen State Print Off. 1948; I and II.

39. Painter RC, Roseboom TJ, Bleker OP. Prenatal exposure to the Dutch famine and disease in later life: An overview. Vol. 20, Reproductive Toxicology. 2005. p. 345-52.

40. Roseboom TJ, van der Meulen JHP, Ravelli ACJ, Osmond C, Barker DJP, Bleker OP. Effects of prenatal expossure to the Ductch famine on adult disease in later life: an overview. Mol Cell Endocrinol. 2001;185(5):93-8.

41. Barker D. Barker-RCIU Article 2011. Bull Acad Natle Méd. 2011;195(3):477-85

42. Elysée C. Bika Lele et al. Prevalence and determinants of blood pressure variability in pygmies of southern region. J Hypertens. 2020; 38:1–8

43. Blacher J, et al. Épidémiologie de l'HTA : différences femme/homme. Presse Med. (2019), https://doi.org/ 10.1016/j.lpm.2019.04.010

44. Gu Q, Burt VL, Paulose-Ram R, Dillon CF. Gender differences in hypertension treatment, drug utilization patterns, and blood pressure control among US adults with hypertension: data from the National Health and Nutrition Examination Survey 1999–2004. Am J Hypertens 2008; 21:789–98.

45. McCarthy A, Hughes R, Tilling K, Davies D, Smith GD, Ben-Shlomo Y. Birth weight; postnatal, infant, and childhood growth; and obesity in young adulthood.pdf. Am J Clin Nutr. 2007;86(4):907-13

Table 1. Sociodemographic and nutritional characteristics of the 2 groups

	Exposed			Unexposed			
	N (total)	**%**	**Mean (SD)**	**N (total)**	**%**	**Mean (SD)**	**p-value**
Age (years)	145		28.2 (3.4)	97		28.6 (3.5)	0.37
Male		57.2			56.7		0.51
Civil status							
Living alone		19.3			21.7		0.74
In a relationship		80.7			78.3		
Ethnic group							
Shi and Havu		99.3			97.9		0.15
Other ethnicities		0.7			2.1		
Religion							
Catholic		45.5			52.6		
Protestant		49.0			46.4		0.39
Other		5.5			1.0		
Level of education							
None		36.6			28.8		
Primary		36.5			28.9		
Secondary		24.8			33.0		0.023
University		2.1			9.3		
Occupational category							
Managerial and administrative position		4.1			14.4		
Farmer + fishermen + market vendor		62.8			61.9		0.011
Unskilled worker		33.1			23.7		
Nutritional survey							
1. Food consumption score							
Inadequate		11.7			11.3		
Borderline		40.0			36.1		0.79
Satisfactory		48.3			52.6		
2. Addition of salt to meals							
Rarely		74.5			81.4		
Often		22.7			14.4		0.23
Always		2.8			4.1		

Table 2. Prevalence of HBP risk factors among the two groups

	Exposed			Unexposed		
	N (total)	**%**	**Mean (SD)**	**N (total)**	**%**	**Mean (SD)***
Anthropometry	145			97		
Height (cm)			158.1 (8.2)			157.7 (8.6)
Weight (kg)			55.2 (7.9)			55.9 (7.2)
BMI° (kg/m^2)			22.1 (2.7)			22.5 (2.6)
<18.5		4.8			4.1	
18.5-24.9		80.7			79.4	
25.0-29.9		13.8			15.5	
>30.0		0.7			1.0	
Cardiovascular risk factors						
1. Alcohol (yes)		49.0			49.5	
2. Tobacco (yes)		4.8			5.2	
3. Family history of HBP[1] and/or diabetes		35.2			36.1	

*For all of the variables, no statistically significant difference was observed between the two groups

[1]HBP=High Blood Pressure.   °BMI=Body Mass Index

Table 3. Clinical and biological markers and prevalence of HBP in the two groups

	Exposed			Unexposed		
	N (total)	%	Mean (SD)	N (total)	%	Mean (SD)*
	145			97		
Blood pressure (BP) mm Hg						
Systolic BP			120.4 (12.1)			120.1 (12.9)
<120		50.3			44.3	
120-139		42.1			49.5	
≥140		7.6			6.2	
Diastolic BP			73.5 (10.3)			75.1 (9.2)
<80		73.1			68.0	
80-89		19.3			23.7	
≥90		7.6			8.3	
Mean BP			89.1 (9.6)			90.0 (9.3)
Pulse pressure			46.9 (10.9)			44.9 (10.6)
High blood pressure		9.7			5.3	
Serum creatinine (mg/dL)			0.91 (0.2)			0.95 (0.2)
0.6-1.4		100.0			94.8	
>1.4		0.0			5.2	

*For all of the variables [except creatinine > 1.4 (p = 0.01)], no statistically significant difference was observed between cases and controls.

Table 4. Difference in Blood Pressure and serum creatinine level between exposed and unexposed

	Unadjusted difference (CI 95%) N*	p-value	Adjusted difference (CI 95%)	p-value
Blood pressure (BP) mm Hg				
Systolic BP	0.4 (-3.2, 4.0)	0.837	0.7 (-2.9, 4.2)	0.72
Diastolic BP	-1.4 (-4.4, 1.4)	0.294	-1.5 (-4.5, 1.4)	0.31
Mean BP	-0.9 (-3.7, 1.9)	0.523	-0.6 (-3.6, 1.9)	0.57
Pulse Pressure	1.9 (-1.2, 5.1)	0.234	2.2 (-1.1, 5.4)	0.18
Creatinine (mg/dL)	-0.04 (-0.07, 0.01)	0.153	-0.04 (-0.09, 0.01)	0.12

Adjusted for BMI, occupational category and food consumption

*N = 145 cases and 97 controls

Table 5: Independent predictors of High Blood Pressure among the total population of the study

	Unadjusted OR (CI 95%) N = 19	p-value	Adjusted OR (95% CI)	p-value
Severe Acute Malnutrition	1.9 (0.7, 5.6)	0.21	3.1 (0.9, 10.9)	0.064
Male	7.1 (1.6, 31.7)	0.010	11.2 (2.2, 55.7)	0.003
Higher Body Mass Index	1.2 (1.1, 1.4)	0.012	1.3 (1.1, 1.6)	0.002
Satisfactory socio-economic status	4.7 (1.3, 16.3)	0.015	3.8 (0.9, 16.3)	0.069
Satisfactory food diversity score	2.3 (0.8, 6.3)	0.10	1.7 (0.5, 5.2)	0.31