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Childhood and infant exposure to famine in the Biafran war is associated with hypertension in later life: The Abia NCDS study

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Ogah OS, Oguntade AS, Chukwuonye II, Onyeonoro UO, Asinobi A, Ogah F, Orimolade OA, Sliwa K, **STEWART S.** Childhood and Infant exposure to famine in the Biafran war is associated with hypertension in later life: The Abia NCDS Study.

Short Title: Exposure to famine in early childhood and hypertension risk

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Word Count:

Abbreviations:

Abia Non-Communicable Disease Study (Abia NCDS)

AME, Average marginal Effect

DBP, Diastolic Blood Pressure

DOHaD, Developmental Origin of Health and Disease

NCDs, Non-communicable Diseases

SBP, Systolic Blood Pressure

ABSTRACT

There are very few studies in Africans investigating the association between early life exposure to malnutrition and subsequent hypertension in adulthood. We set out to investigate this potential association within an adult cohort who were born around the time of the Biafran War (1968-1970) and subsequent famine in Nigeria.

This was a retrospective analysis of Abia State Non-Communicable Diseases and Cardiovascular Risk Factors (AS-NCD-CRF) Survey, a community-based, cross-sectional study that profiled 386 adults (47.4% men) of Igbo ethnicity born in the decade between January 1965 and December 1974. Based on their date of birth and the timing of the famine, participants were grouped according to their exposure to famine as children (Child-Fam) or in-utero fetus/infant (Fet-Inf-Fam) or no exposure (No-Fam). Binomial logit regression models were fitted to determine the association between famine exposure and hypertension in adulthood.

Overall, 130 participants had hypertension (33.7%). Compared to the No-Fam group (24.4%), the prevalence of hypertension was significantly elevated in both the Child-Fam (43% - adjusted OR 2.47, 95% CI 1.14-5.36) and Fet-Inf-Fam (44.6% - adjusted OR 2.54, 95% CI 1.33-4.86) groups. The risk of hypertension in adulthood was highest among females within the Child-Fam group. However, within the Fet-Inf-Fam group males had a equivalently higher risk than females .

These data suggest that early life exposure to famine and malnutrition in Africa is associated with a markedly increased risk of hypertension in adulthood; with sex-based differences evident. Thus the importance of avoiding armed conflicts and food in-security in the region cannot be overstated. The legacy effects of the Biafran War clearly shows the wider need for ongoing programs that support the

nutritional needs of African mothers, infants and children as well as proactive surveillance programs for the early signs of hypertension in young Africans.

Keywords: famine, fetal-infant malnutrition, Barker's hypothesis, hypertension, Biafra, civil war

INTRODUCTION

Early life and childhood malnutrition have been linked with future increased risk of cardiovascular diseases in adulthood in experimental models.[1,2] Moreover, follow-up studies from survivors of the Dutch famine and the Leningrad siege provide evidence for the role of fetal and childhood undernutrition in cardiovascular diseases in middle age.[3–7] This phenomenon has been aptly explained by the Barker hypothesis.[8–10] Fetal malnutrition leads to a 'thrifty' phenotype in extra-uterine life and a mismatch with the environment during periods of food abundance with resultant accumulation of salt and insulin resistance which leads to increased risk of hypertension and diabetes.[11]

Children in sub-Saharan Africa and many other developing countries continue to suffer and die from malnutrition.[12,13] This is exacerbated by regional conflicts, wars and insurgencies leading to displacement of people, severe disruption of food supplies and poverty. Furthermore, many of these countries are steadily advancing in the epidemiologic transition of diseases and are now facing a double burden of communicable and non-communicable diseases (NCDs). About a third of adults in Nigeria have hypertension which remains uncontrolled in about half of these individuals leading to increased incidence of stroke and resultant morbidity and mortality.[14] This significantly affects the productivity of the active workforce and has enormous economic implications.

Historical conflicts may play an important role in the high prevalence of hypertension in African countries like Africa. However, there are very few studies investigating the impact malnutrition and famine exposure early in life on the subsequent cardiovascular health of African men and women. Hult and colleagues[15] previously revealed an increased risk of hypertension and diabetes in adulthood among Igbo residents of Enugu, South-eastern Nigeria, born during the Nigerian civil war (1967-1970) - also known as the ***Nigeria-Biafra War***. This phenomenon represents a natural experiment to

investigate the Developmental Origin of Health and Disease (DOHaD)[16] framework and the Barker hypothesis[10] in those of African ancestry.

Within this context, we aimed to determine the association between famine exposure in early life and hypertension in adulthood by analyzing data from a previous community-based survey conducted in the East-African country of Nigeria. We hypothesized that individuals born or in early childhood during the *Nigeria-Biafra War* (Biafran War) that occurred from July 1967 to Jan 1970 who were subsequently exposed to famine conditions, would have a higher risk of hypertension in adulthood when compared those born in the five-years following the war.

METHODS

This represents a secondary analysis of data collected as part of the Abia State Non-Communicable Diseases and Cardiovascular Risk Factors (AS-NCD-CRF) Survey. Described in more details previously [17,18], the study comprised a community-based, household survey of people aged ≥15 years living in the southeastern Nigerian State of Abia. For this study, we purposefully focused on study participants of Igbo ethnicity who were born before, during and following the famine that was triggered by Biafran War. The study was approved by the Abia State Ministry of Health Ethics Review Committee and all the participants provided informed consent, in accordance with the Declaration of Helsinki.[19]

The Nigerian Civil War and the Famine in Eastern Nigeria

In brief, the Biafran War was triggered in July 1967 following the secession of the Eastern region of Nigeria as an aftermath of ethnic tensions and pogroms in different parts of the country and the failure of the Aburi accord.[20] The Nigerian government started a “police” offensive initially to halt the secession. This resulted in a full war that led to the opposing Biafran forces being pushed back into a small enclave.[21] With basic supplies purposefully cut-off from the populace living in the enclave of

105 Biafra, one of the worst humanitarian crises in Africa developed.[21,22] Under difficult circumstances,
106 including interference by both warring parties, famine relief operations were then undertaken by the
107 International Committee of the Red Cross. However, more than 2 million people (including around a
108 million children) died during the conflict, with famine and kwashiorkor major causes of death.[21 21 21]
109 The war and accompanying famine conditions finally ended in January 1970 following the surrender of
110 the Biafran forces and the end of the supply blockade.[15] **Figure 1** below depicts the birth cohort and
111 Biafran famine in the study period.

112 **Setting and Participants**

113 The AS-NCD-CRF was conducted between August 2011 and March 2012. A multistage stratified cluster
114 sampling was used to select participants from each of the three senatorial districts in Abia State.[18]
115 Briefly, one rural and one urban local government area (LGA) was randomly selected from Ohafia and
116 Isuikwuato/Bende (Northern), Umuahia North and Ikwuano (Central) and Aba South and Ukwa East
117 (Southern Senatorial Zone).[18]

118 In each LGA, households and their eligible participants within four randomly selected Enumeration
119 Areas were selected for profiling. Starting from a prominent landmark in the community, trained
120 interviewers proceeded from household to household to interview a minimum of 120 eligible
121 participants in the area. Data were collected using the WHO-STEPwise approach surveillance
122 questionnaire.

123 **Study Data**

124 Once selected, participants were asked about their year of birth, their level of education, smoking,
125 alcohol consumption, exposure to stress, family history of cardiovascular disease, previous diagnosis of
126 hypertension, diabetes, cancers, asthma and any other NCDs.[17] There was no information on

participants' birth weight. They were also weighed using a weight balance and also had their height measured.[18] Body mass index (BMI) was then calculated (kg/m^2) and categorized according to WHO thresholds.[23] Waist and hip circumference were measured using the WHO methodology.[23,24] Blood pressure (BP) measurements were performed with an Omron Digital BP device (Omron M2 BP monitor - Tokyo Japan) following a 5-minute resting period. Three BP reading at 2 minutes intervals were taken; the average of the second and third readings was used for analysis. Systemic hypertension was defined as SBP≥140 mmHg and or DBP≥90 mmHg or normal SBP and DBP in a subject using antihypertensive treatment.[18]

Famine Exposure

The conflict induced famine in Biafra mainly occurred from January 1968 to January 1970 (**Figure 1**). Accordingly, study participants were categorized into three different exposure groups/birth cohorts based on their birth date relative to this specific period. Firstly, those born in the pre-famine period of January 1965 to December 1967 were categorized as being exposed to famine in their early childhood (Child-Fam group). Those born during the specific famine period were categorised as the fetal/infant exposure (Fet-Inf-Fam) group. Individuals born in the transitional period between February 1970 and December 1970 were excluded from the analysis due to uncertainties about their nutritional status. Lastly - identify and the define the 3rd non-exposure group (No-Fam) group!!!

Statistical Analysis

The distribution of data was tested using the Shappiro-Wilk test and histogram plots. Data are presented as mean (SD), proportions (%) and odds ratio (OR) with 95% confidence intervals (CI) as appropriate. Differences between groups were tested using one-way ANOVA for continuous variables and chi square and exact test for categorical variables. Logistic regression models were used to

investigate the association between hypertension in adulthood and famine exposure status. These models were also adjusted for age, sex, smoking, stress, education, and BMI. We investigated the interaction between sex and exposure to famine on hypertension risk in separate analyses since associations between early life exposures and cardiovascular risk have been shown to vary with gender using the sex × famine exposure status interaction terms. We also investigated possible interaction between sex and BMI, but this was not significant in adjusted model. We further fitted logit regressions to estimate the marginal effects at the mean (MEM) and average marginal effects (AME) by regressing hypertension on exposure to famine and potential explanatory variables. We did this to estimate the predicted probabilities of hypertension in relationship to exposure to famine at different stages of development, and other explanatory variables. The coefficients of the MEM and AME shows the change in probability of hypertension occurring with a unit change in famine exposure while keeping the other covariates within the sample at their means or their individual values respectively. The marginal effect is the difference in the adjusted predictions between each category of famine exposure and the reference unexposed group. The fitted models were robust to the addition of the different explanatory variables and the fully adjusted model is presented. The coefficients of the MEM and AME were comparable and so only the latter are presented. We also plotted the predictive margins of famine exposure and risk of hypertension in adulthood. All data were analyzed using Stata version 17 (StataCorp LLC, Lakeway Drive, College Station, Texas, USA) with plots generated using the Stata and Jasper package (by Matt Arnold) in R version 4.1.3 (R Foundation for Statistical Computing, Vienna, Austria). A two-sided p-value of <0.05 was considered statistically significant in all analyses while clinical importance was based on the magnitude and direction of effect sizes and 95% CI's.

RESULTS

Cohort Characteristics

Table 1 summarizes the profile of study participants' according to the three pre-specified famine exposure groups. Of the 386 participants studied overall, 93 (21.6%) were included in the Child-Fam group, 92 (21.3%) in the Fet-Inf-Fam group and the remaining 201 (46.6%) participants in the No-Fam group, with age-gradients reflecting their year of birth. Overall, there was no difference in education status, smoking or alcohol consumption between groups. However, the Child-Fam group exhibited lower central adiposity compared to the other two groups; despite their being no difference in mean BMI between the three groups (all being the overweight range). Reported exposure to stress in adulthood was significantly higher (78.3%) in the Fam-Child group compared to the Fet-Inf-Fam and No-Fam groups (58.2% and 59.4%, respectively); p=0.01 for the comparison.

Blood Pressure Profiles

Compared to the No-Fam group (24.4%), the prevalence of hypertension was significantly elevated (p=0.001) in both the Child-Fam (43%) and Fet-Inf-Fam (44.6%) groups - see **Table 1.** Consistent with this observation, SBP/DBP levels were significantly higher in the Child-Fam and Fet-Inf-Fam groups. When compared to the No-Fam reference group, the Child-Fam group had a 2.8-fold increased risk of an elevated SBP when adjusting for potential biological and lifestyle confounders. On the same basis, the Fet-Inf-Fam group had an adjusted 1.8-fold risk of an elevated SBP. A similar pattern of higher adjusted risk for elevated DBP, was also found in the these two groups – see Table 2.

Hypertension

On a crude and then adjusted basis, individuals within the Child-Fam group were 2.3-fold and 2.5-fold more likely to have hypertension in adulthood when compared to the No-Fam group. Similarly, the

same crude and adjusted risk of hypertension in adulthood within the Fet-Inf-Fam groups was 2.5-fold than the No-Fame group.

As shown in **Figure 3**, on a sex-specific basis, after adjustment for potential confounders, within the women (adjusted OR 2.75, 95% CI 1.02-7.41) in the Child-Fam group had a higher risk of hypertension than their male counterparts (OR 2.23, 95% CI 0.55-9.00) when compared to the No-Fam group. Within the Fet-Inf-Fam group, however, this sex-specific trend was reversed with men having a higher adjusted risk than women of having hypertension in adulthood.

Figure 4 presents a forest plot showing the AME of hypertension probability in adulthood. Individuals within the Child-Fam and Inf-Fet-Fam groups had similar predicted probability of hypertension in adulthood; being 20% higher than No-Fam group in adjusted analyses. There was a steep increase in hypertension prevalence with famine exposure, with the highest levels found in the Child-Fam Group. This observed increased risk for hypertension was stronger in women than in men. Overall, on an adjusted basis, individuals within the Child-Fam and Fet-Inf-Fam were at increased risk of hypertension compared to the No-Fam group.

As shown in **Table 3**, the AME of hypertension showed a higher predicted probability in women compared to men (22% vs. 16%) within the Child-Fam group compared to the No-Fam group. Similarly, within the Fet-Inf-Fam group, men had a slightly higher predicted probability of hypertension (21% vs. 19%) than women. The predictive margins of the sex-specific hypertension risk in the 3 study groups/birth cohorts is shown in **Figure 5 below**. There was a steep increase in hypertension prevalence with famine exposure which was highest in the Child-Fam group. This increased risk was stronger in women than men within both the Child-Fam and Fet-Inf-Fam groups. The time trend in the risk of hypertension by birth year over the 10 years spanning 1965-1974 is presented in **Figure 6**. Two

peaks of hypertension risk can be seen in those born in 1965 and those born in 1968 at the peak of famine. Thereafter, the risk of hypertension declined.

DISCUSSION

The famine triggered by the Biafran War was a humanitarian disaster. Its legacy continues to haunt Nigeria. In this study, we specifically investigated the risk of hypertension in adulthood among those born in the decade before, during and following the famine. We sought to test and validate the DOHaD framework[16] and the Barker's hypothesis[8,9]; both of which suggest that early life and intrauterine adverse events like malnutrition leads to developmental programming towards vascular diseases later in life. Accordingly, we found an elevated, adjusted risk of adult hypertension within both the Child-Fam and Fet-Inf-Fam groups compared to those born after the famine (No-Fam group). However, we found no evidence to support the pathway postulated by DOHaD[16,25] that early life malnutrition may influence access to education, future socio-economic status, lifestyle and substance consumption. [16,25] Adjusting for lifestyle variables, including emotional stress, did not significantly mediate the increased risk of hypertension among those exposed to famine. Nor was there an association between lifestyle variables and famine exposure. This contrasts with recent findings by Mink *et al*.[25] in the French E3N cohort and the reports by Fransen and colleagues.[25] Furthermore, in contrast to reports from Jyoti and colleagues[26] and Akresh and colleagues[22] we also did not find any association between famine exposure in early life and educational attainment among those who lived through the Biafran War.

The latency framework of the DOHaD proposes a direct link between early life famine exposure and hypertension in adulthood through epigenetic re-programming.[16,25] We sought to explain the role of biological sex in hypertension risk among the famine exposure groups. Within the Child-Fam group, women showed a trend of towards a higher risk of hypertension compared to men, with this pattern

reversed within the Fet-Inf-Fam group. Those who experienced famine in childhood and those with fetal-infant malnutrition had similar Overall, the predicted probability of hypertension (20% higher than the No-Fam group) was similar for the two famine exposed groups. However, there was a markedly higher (6% more) predicted probability of hypertension in women than men within the Child-Fam group. Alternatively, within the Fet-Inf-Fam group, the predicted probability of hypertension tended to be higher in men.

Evidence for sex-based differences in the association of early adverse life events and BP have been weak with a meta-regression analysis finding no sex difference in the association between birth weight and systolic BP in later life.[27] Hult and colleagues[15] did not find significant sex differences in risk of hypertension after exposure to the Biafra famine in their study of market subjects in Enugu, Nigeria; even though the average risk of hypertension reported is comparable to ours.[15] It appears that African women are more susceptible to hypertension when they experience malnutrition in childhood. Alternatively, African men appear to be more susceptible to the effects of malnutrition in-utero. These observations are consistent with those of Kuopil and colleagues[28] who studied childhood survivors of the extreme starvation experienced during Leningrad siege in Russia. We may also explain the higher risk in women exposed to malnutrition in childhood by the observation made by Akresh and colleagues.[22] that women exposed to the war in their growing years exhibited more stunting, higher overweight risk, earlier age at first birth and lower educational attainment. It is now well established that the first 12 weeks of pregnancy (the embryonic period) is very critical to future health risk. This is the period when organs like the kidneys, heart and blood vessels are forming.[29,30] Low birth weight followed by accelerated weight gain in the age group 3-11 years predicted a large difference in the cumulative incidence of hypertension in adulthood in the Helsinki birth cohort.[8] Hypertension may

originate from retarded in-utero growth followed by accelerated postnatal growth when exposed to good living conditions.[31] Males who suffer intra-uterine growth restriction are more likely to be born with smaller organs and fewer glomeruli as propounded by David Barker[3,10] and would thus be at high risk of hypertension later in life as shown in our study. There appears to be some specific expression of fetal genes critical to developmental programming in-utero especially when exposed to stress and growth restriction in the early weeks of fetal development.[32–34] Females may be protected by their two X chromosomes unlike males who have only one X chromosome.[35] Protein-energy malnutrition and even small variations in the balance of macronutrients in maternal diet during pregnancy and/or lactation alters BP control of such children through central sympathetic dysfunction and epigenetic modification like hypomethylation of genes e.g. angiotensin II type I receptor and IL-6 genes.[36,37] Moreover in experimental models, there is increased hypoxia inducible factor-1α (HIF-1α) expression in the carotid bodies, hearts and brains of rats exposed to protein-energy malnutrition during pregnancy and/or lactation. High HIF-1α expression is associated with increased risk of hypertension and enhanced activity of peripheral chemoreceptors.[37]

Risk of hypertension is programmed by prenatal and early postnatal experiences with poor maternal nutrition playing key role by restraining fetal growth. Sesso and colleagues[13] have shown the role of childhood malnutrition in increased hypertension risk independent of birth weight. Similar findings have been reported from Brazil.[38] Furthermore, reports of survivors of the Leningrad siege[28], the Great Chinese famine[39] and the Dutch famine[4,5] have previously confirmed the increased risk of hypertension in those with malnutrition in fetal and childhood periods. Malnutrition in early life could initiate hypertension in adulthood by activation of the renin-angiotensin-aldosterone system, alteration in vascular structure and function, increased sympathoadrenal activity, associated increased heart rate,

281 elevated urinary catecholamines, and reduced vascular compliance.[13] Alternatively, other researchers[3]
282 have failed to show an association between prenatal famine exposure and hypertension in adulthood.
283 We found a much higher predicted probability of hypertension (20% higher) among those exposed to
284 famine in our cohort when compared to an equivalent report of 2.6% higher reported by Mink and
285 colleagues.[25] This may be because they were unable to distinguish between those did and didn't
286 experience hunger in childhood within their cohort.[25] By assuming that everyone born in certain
287 periods experienced malnutrition, we may have overestimated the average marginal effects. However,
288 famine was endemic in Biafra during the period 1968-1970 when food supplies were completely shut-
289 off and Biafran lands were unsuitable for cultivation of protein crops.[15,20,21] Consequently, over 2
290 million children developed kwashiorkor and marasmus with more than 1 million children subsequently
291 dying.[20] Our finding of a higher risk and predicted probability of hypertension in females exposed to
292 famine in childhood compares with previous reports from the survivors of the Leningrad siege.[28] –
293 consider remove or place back into sex-specific section
294 Overall, our result supports a strong association between early life exposure to famine and the
295 development of hypertension in adulthood. Mismatch between the food sufficiency of today's eastern
296 Nigeria and the famine of the 60s may be contributory to the rise in hypertension and stroke-related
297 events observed in eastern Nigeria. We have also shown the sex differences in hypertension risk based
298 on the time of famine exposure during development with the highest risk in males exposed in utero
299 and the highest risk in females exposed during childhood. These findings are especially important
300 today when Nigeria is facing terrorist insurgency in the Northern part of the country with millions
301 displaced from their houses and lands.[40] The victims of the present insurgent crisis are also now facing
302 critical food shortages resulting in childhood malnutrition. In simple terms, preventing such conflicts

and consequent famine/malnutrition early in life will improve long-term cardiovascular health and improve life-expectancy in many parts of the Africa continent.

The study is not without limitations. It is a cross sectional study and it is difficult to ascertain causality even though we have tried to adjust for important biological and behavioural factors. We assumed that all those born during the period 1965-1970 were automatically exposed to famine and protein-energy malnutrition. This may have led us to overestimate the effects sizes. We were also unable to distinguish between exclusively in-utero versus infant exposure to famine within the cohort. Consequently, our analyses may underestimate the effects of malnutrition in the fetal period given the overlap in famine exposure during infancy (with potentially no exposure to famine in-utero). We were also unable to investigate the effects of malnutrition in different stages of gestation. Of relevance here is the absence of birth weight records and subsequent childhood anthropometric profiling data to more rigorously explore the likely degree and legacy effects of malnutrition exposure in each individual. This is a common problem in developing countries like Nigeria where such historical records are typically non-existent. Although we collected BP data, it was derived from one time-point. This could have led us to overestimate the prevalence of hypertension. Another concern is the validity of estimates if there had been a change in the Biafran population composition due to differential mortality of the least healthy and most vulnerable to famine, then this would have led to underestimation of our effect sizes.

Despite these limitations, the strength of the study lies in its focus on a homogenous Igbo population and statistical analyses that generated risk prediction and measurement of potential sex differences in the risk of hypertension in adulthood while controlling for biological and lifestyle variables. Our findings suggest that behavioural lifestyle factors do not play an appreciable role in the association of

famine with hypertension in adult life. We were able to demonstrate the direct latency pathway of the DOHaD.[16,25] We also showed a higher risk of hypertension exposed to famine in-utero exposure, whilst also showing that the highest risk of famine exposure (in respect to hypertension later in life) occurred in females aged under 5-years. Early life exposure to malnutrition (whether it be as a result of conflict or economic factors) has a long-term, negative legacy effect. To invest in the future of African children and future economic prosperity, therefore, there needs to be a concerted effort to support school feeding programmes alongside proactive health screening programs. This is particularly true in current parts of Nigeria where the threat of insurgency and food insecurity are tragically all too common still.

Acknowledgements

The authors thank all the research assistants who participated in the survey.

Competing interests

The authors declare no competing interests.

List of figures

Figure 1: Schematic presentation of Biafra famine and birth cohort

Figure 2: Forest plot of crude model of famine exposure and hypertension in adulthood

Figure 3: Forest plot of adjusted model of famine exposure and hypertension in adulthood

Figure 4: Forest plot of average marginal effects (AME) of hypertension in adulthood

Figure 5: Plot of the predictive margins of the interaction between sex and famine exposure and risk of hypertension in adulthood

Figure 6: Temporal trend of hypertension risk at follow up in 2010 according to year of birth and with 1974 as reference

Figure 7: Take Home Message: Exposure to Famine in Early Life and Risk of Hypertension in Mid-Life in Survivors of the Biafran Famine

List of tables

360 **Table 1** shows the study participants' clinical characteristics of the two groups exposed to famine and

361 the unexposed group.

362

Variable	Born 01 Jan 1965-31Dec. 1967 Childhood famine	Born 01 Jan 1968- 31 Jan 1970 Fetal-infant famine	Born 01 Jan 1971- 31 Dec 1974 Unexposed to famine	P value
Number of subjects (431)	93 (21.6%)	92 (21.3%)	201 (46.6%)	
Sex (male) %	47 (50.5%)	50 (54.3)	86 (42.8)	0.15
Age (years)	45.1 (3.9)	42.4 (3.3)	38.4 (2.2)	<0.001**
Smoking (%)	4 (4.3)	7 (7.7)	22 (10.9)	0.16
Alcohol (%)	59 (63.4)	54 (58.7)	113 (56.2)	0.51
Education (%)				
Below secondary	26 (28.0)	27 (29.4)	52(25.9)	0.81
Secondary and above	67 (72.0)	65(70.6)	149 (74.1)	
Feeling stressed %	72 (78.3)	53 (58.2)	117 (59.4)	<0.01*
Family history of CVD	39 (41.9)	33 935.9)	73 (36.3)	0.61
Hypertension (%)	40 (43.0)	41 (44.6)	49 (24.4)	<0.001**
Weight (Kg)	71.1 (15.8)	72.4 (14.0)	69.8 (12.8)	0.07
Height (cm)	163.2 (9.7)	164.9 (8.5)	163.5 (8.4)	0.22
BMI ($Kg/m^{2)}$	26.6 (5.3)	26.5 (4.9)	25.8 (4.5)	0.19
Waist circumference (cm)	86.2 (14.2)	88.1 (16.0)	88.2 (23.4)	<0.001**
Hip circumference (cm)	95.3 (14.9)	97.9 (14.3)	95.0 (17.5)	0.05

Hip-waist ratio	1.0 (0.2)	1.1 (0.1)	1.1 (0.3)	<0.001**
Heart rate (beats/min)	78.3 (11.4)	77.0 (10.0)	77.2 (10.4)	0.51
Systolic BP (mmHg)	135.3 (29.5)	131.3 (21.0)	126.0 (28.5)	<0.01*
Diastolic BP (mmHg)	80.6 (15.7)	79.6 (14.1)	75.6 (17.4)	0.07

363 * p value <0.05; **p value ≤0.001

364

Table 2: Odds ratio for hypertension (reference category is the unexposed group).

			All subjects N=386	N=330
Variables	N	n (%)	Crude OR	Adjusted OR
SBP ≥140mmhg	386	102 (26.4)		
Childhood	93	36 (38.7)	2.80 (1.62-4.85)	2.85 (1.26-6.44)
Fetal-infant	92	29 (31.5)	2.04 (1.16-3.59)	1.76 (0.88-3.53)
Unexposed	201	37 (18.4)	Ref.	Ref.
DBP ≥90mmhg	386	85 (22.0)		
Childhood	93	26 (28.0)	2.05 (1.14-3.70)	2.57 (1.06-6.19)
Fetal-infant	92	27 (29.3)	2.19 (1.22-3.94)	2.73 (1.30-5.73)
Unexposed	201	32 (15.9)	Ref.	Ref.
Hypertension	386	130 (33.7)		
Childhood	93	40 (43.0)	2.34 (1.39-3.94)	2.47 (1.14-5.36)
Fetal-infant	92	41 (44.6)	2.49 (1.48-4.20)	2.54 (1.33-4.86)
Unexposed	201	49 (24.4)	Ref.	Ref.

SBP: systolic blood pressure, DBP: diastolic blood pressure, HTN: hypertension.

Adjusted model includes famine exposure groups, sex, present age, education attainment (secondary education and above vs. below secondary education), family history of cardiovascular disease, smoking status (Yes vs. No), feeling stressed (Yes vs. No) and body mass index (BMI)

Table 3: Average marginal effects of hypertension stratified by sex (fully adjusted model)

Famine exposure	Average marginal effects (AME); 95%CI	P value
Childhood famine		
Female	0.22 (0.00; 0.44)	0.05
Male	0.16 (-0.12; 0.44)	0.27
Fetal-Infant famine		
Female	0.19 (-0.01; 0.39)	0.06
Male	0.21 (0.01; 0.42)	0.04

Adjusted model includes famine exposure groups, sex, present age, education attainment (secondary education and above vs. below secondary education), family history of cardiovascular disease, smoking status (Yes vs. No), feeling stressed (Yes vs. No) and body mass index (BMI)

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