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Childhood famine exposure and the risk of gastrointestinal diseases in old individuals: a retrospective cohort analysis using the CHARLS database

Qingquan Yang[1*†] and Zhiyuan Rong[1*†]

Abstract

Background The aging of the global population exacerbates the burden of gastrointestinal diseases in elderly individuals. The Developmental Origins of Health and Disease (DOHaD) hypothesis suggests that early-life malnutrition may have long-lasting effects on adult health. However, evidence regarding the link between childhood famine exposure and the risk of gastrointestinal diseases in old individuals remains limited.

Methods We conducted a retrospective cohort study of 4227 participants from the China Health and Retirement Longitudinal Study (CHARLS). Childhood famine exposure was defined as experiencing hunger before age 18 during the 1959–1961 famine period. The outcomes were doctor-diagnosed gastric or other digestive diseases. Logistic regression, propensity score matching (PSM), subgroup analysis, and XGBoost machine learning with SHAP explanation were used.

Results A total of 83.7% of the participants had childhood famine exposure. The famine-exposed group had a significantly higher risk of gastrointestinal diseases (OR = 1.34, 95% CI: 1.12–1.61); this association persisted after PSM (OR = 1.39, 95% CI: 1.10–1.75). Subgroup analysis yielded consistent results (all P values for interactions > 0.05). Famine exposure was identified as an important predictive factor in the XGBoost machine learning algorithm.

Conclusions Childhood famine exposure is significantly associated with an increased risk of gastrointestinal diseases in old individuals. This simple indicator should be included in regular health assessments for the elderly to facilitate early identification and intervention for high-risk populations.

Keywords Childhood famine, Gastrointestinal diseases in the elderly, DOHaD hypothesis, CHARLS database, XGBoost

†Qingquan Yang and Zhiyuan Rong contributed equally as corresponding authors.

*Correspondence:
Qingquan Yang
yqqsy@163.com
Zhiyuan Rong
rongzhiyuan98@163.com
[1]The Second Affiliated Hospital of Shenyang Medical College, Shenyang 110801, China

Introduction

The global population is aging at an unprecedented rate, profoundly impacting global public health systems. The number of people aged 60 and above is projected to double from approximately 1 billion in 2020 to 2.1 billion by 2050, with the majority residing in low- and middle-income countries [1]. This demographic shift has intensified the burden of age-related chronic diseases, particularly gastrointestinal disorders, which are among the most common health challenges in the elderly [2, 3]. Common gastrointestinal problems in elderly individuals, such as inflammatory bowel disease, motility disorders, and malnutrition-related complications, not only impair quality of life but also lead to increased healthcare utilization and mortality rates [4]. Lifelong epidemiology emphasizes that health outcomes in later years are strongly influenced by cumulative exposure throughout life, with early adversity laying the foundation for susceptibility to chronic diseases in old age [5, 6].

Evidence for this theory can be found in the Developmental Origins of Health and Disease (DOHaD) hypothesis, which posits that environmental insults during critical windows of early development, including the fetal and postnatal periods, may induce epigenetic reprogramming, metabolic adaptation, and structural changes in organs, increasing susceptibility to chronic noncommunicable diseases in adulthood [7, 8]. Historical famine events, such as the Dutch Hunger Winter (1944–1945) and the Chinese Great Famine (1959–1961), serve as quasi-experimental models to test the DOHaD framework, as they represent acute periods of nutritional deprivation that can isolate the effects of early malnutrition from other confounding factors [9, 10]. These events have played a key role in elucidating how malnutrition during pregnancy and childhood can imprint metabolic disorders and organ dysfunction over the long term [11, 12].

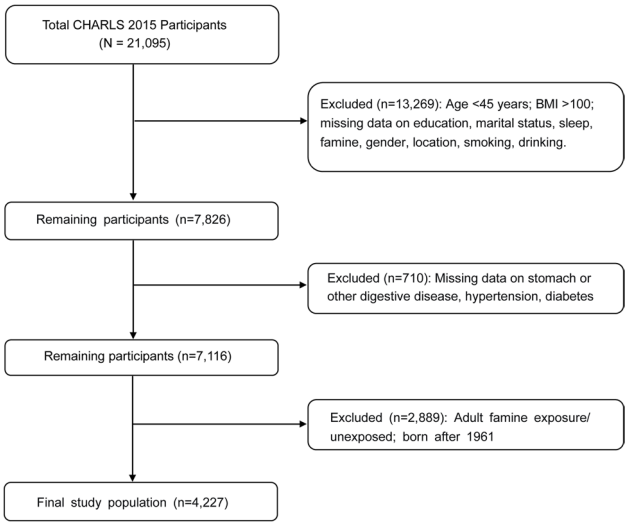

Fig. 1 Flow diagram of participants

Studies have linked early famine exposure to various adverse health outcomes in later life, including an increased risk of metabolic syndrome, cardiovascular diseases, and cognitive impairment [13–15]. The digestive system, as the primary interface for nutrient absorption and the first line of defense against environmental stress, may be particularly sensitive to such early insults, leading to long-term changes in the gut microbiome, impaired mucosal integrity, and motility dysfunction [16]. However, despite these insights, there is limited research specifically investigating the association between childhood famine exposure and gastrointestinal disease incidence in old individuals [17].

Therefore, this study aims to use nationally representative CHARLS data to explore the association between childhood famine exposure and the incidence of gastrointestinal diseases in old individuals. We hypothesize that early-life nutritional stress significantly increases the risk of gastrointestinal dysfunction later in life.

Methods

Study population

This was a retrospective statistical analysis of the China Health and Retirement Longitudinal Study (CHARLS) data. The CHARLS is a longitudinal study of Chinese individuals aged 45 years and above that includes demographic characteristics, lifestyle, and health data [18]. CHARLS received approval from the Institutional Review Board of Peking University, and informed consent was obtained from all participants.

This study used CHARLS data from 2011, 2013, 2014, and 2015. We established the 2015 data as our baseline and merged information from the 2011 and 2013 waves for participants with documented diagnoses of hypertension, diabetes, or gastrointestinal diseases. Famine exposure data were obtained from the 2014 survey wave. Participants under 45 years old, born after 1961, or with missing data were excluded, leaving 4,227 participants for analysis (Fig. 1).

Definition of childhood famine exposure

Participants who were under 18 years of age during the famine period (1959–1961), meaning born between 1941 and 1961, and who answered "yes" to the question "Between 1958–1962 did you and your family (including your grandparents, parents, siblings, children, etc.) experience starvation?" in the 2014 questionnaire were defined as having childhood famine exposure. Additionally, to examine stage-specific effects, we stratified exposure into early childhood (< = 12 years during famine) and adolescence (13–18 years during famine).

Definition of Gastrointestinal disease

Participants who answered "yes" to the question "Have you been diagnosed with stomach or other digestive diseases (except for tumors or cancer) by a doctor?" In any survey wave between 2011 and 2015, patients were classified as having gastrointestinal disease (excluding tumors or cancer).

Covariate assessment

Sociodemographic and health-related variables were collected through a system questionnaire administered by trained interviewers. Sociodemographic characteristics included age, gender (female, male), location (city, village), education level (less than high school, high school, university completed or above), and marital status (married, divorced, unmarried). The health-related behavior indicators included smoking status (yes, no), drinking (none of these, drink but less than once a month, drink more than once a month), BMI, and sleep time. When asked "Have you ever chewed tobacco, smoked a pipe, smoked self-rolled cigarettes, or smoked cigarettes/cigars?" Those who answered "yes" were classified as smokers. Participants were classified as underweight (< 18.5 kg/m2), normal (18.5–23.9 kg/m2), overweight (24–27.9 kg/m2), or obese (≥ 28 kg/m2) on the basis of BMI [19]. A history of chronic diseases, including hypertension and diabetes, was confirmed by clinical diagnosis.

Statistical analysis

Descriptive statistics were used to summarize baseline characteristics by exposure status. Continuous variables are presented as mean and standard deviation (SD), and categorical variables are presented as counts and percentages. Group comparisons were made via nonparametric tests or chi-square tests.

Multivariable logistic regression was used to develop three models: Model 1 (unadjusted), Model 2 (adjusted for age, gender, education, location and marital status), and Model 3 (adjusted for all covariates).

Propensity score matching (PSM) was applied to control for baseline differences between the exposed and unexposed groups. We used a 1:1 nearest-neighbor matching method (caliper = 0.2) and fitted a logit model using all covariates as independent variables to estimate the propensity score.

Subgroup analysis was performed by categorizing covariates into different subgroups (age, gender, education, marital status, location, smoking, drinking, sleep, BMI, hypertension, and diabetes) and including interaction terms to test for heterogeneity in the effect of childhood famine exposure on gastrointestinal diseases.

Machine learning and model interpretability were assessed via XGBoost to construct a classification model for predicting gastrointestinal disease. To overcome the "black box" nature of machine learning models, SHAP (SHapley Additive exPlanations) values were calculated via "SHAPforxgboost" and "shapviz" to quantify the marginal contribution of each feature to the model output. Feature importance rankings (mean(|SHAP|)) were reported on the basis of matched and unmatched datasets, and SHAP dependency plots were used to visualize the complex relationships between feature values and outcome risk.

Results

Baseline characteristics

Among the 4,227 participants, 3,537 (83.7%) had childhood famine exposure. Table 1 shows that, before matching, there were significant differences between the exposed and unexposed groups in terms of age, gender, location, and gastrointestinal diseases ($p < 0.05$). After PSM, 690 pairs of individuals (total $n = 1{,}380$) were successfully matched. After matching, most covariates were well balanced (Table 2), although residual differences in age and gender persisted and were appropriately adjusted for in subsequent analyses.

Association between famine exposure and Gastrointestinal diseases in old individuals

We used three logistic regression models to analyze the relationship between childhood famine exposure and gastrointestinal diseases in in old individuals. In all the models, we found a significant association between childhood famine exposure and a higher risk of gastrointestinal diseases. Model 1: OR = 1.34 (95% CI: 1.12–1.61, $p = 0.002$); Model 2: OR = 1.37 (95% CI: 1.14–1.65, $p < 0.001$); Model 3: OR = 1.36 (95% CI: 1.13–1.63, $p = 0.001$) (Table 3). After PSM, the association remained robust and slightly strengthened: OR = 1.39 (95% CI: 1.10–1.75, $p = 0.005$) (Table 4). Stage-specific analysis indicated that famine exposure during adolescence was not significantly associated with gastrointestinal diseases in old age, compared to exposure during early childhood (Model 1: OR = 1.05 (95% CI: 0.88–1.25, $p = 0.6$); Model 2: OR = 1.08 (95% CI: 0.83–1.41, $p = 0.6$); Model 3: OR = 1.09(95% CI: 0.83–1.43, $p = 0.5$)) (Supplementary Table 1).

Subgroup analysis

We performed stratified analyses to examine the associations between childhood famine exposure and gastrointestinal diseases in different subgroups. The results of the subgroup analysis were highly consistent. In most subgroups, childhood famine exposure was positively associated with the risk of gastrointestinal diseases, and the interaction terms were not significant (all P values for interactions > 0.05; variables included age, gender, education, marital status, location, smoking, drinking, sleep, BMI, hypertension, and diabetes) (Fig. 2). The results of

Table 1 Baseline characteristics of the participants

Characteristic	Overall *N* = 4227	Famine exposed *N* = 3537	Famine unexposed *N* = 690	*p*-value
Age, years	63.1 ± 5.4	63.2 ± 5.3	62.5 ± 5.6	0.001
Gender, n(%)				0.001
Female	3429 (81.1%)	2838 (80.2%)	591 (85.7%)	
Male	798 (18.9%)	699 (19.8%)	99 (14.3%)	
Education, n(%)				0.467
College completed or above	8 (0.2%)	6 (0.2%)	2 (0.3%)	
High school	3335 (78.9%)	2781 (78.6%)	554 (80.3%)	
Less than high school	884 (20.9%)	750 (21.2%)	134 (19.4%)	
Marital status, n(%)				0.210
Divorced	573 (13.6%)	471 (13.3%)	102 (14.8%)	
Married	3641 (86.1%)	3057 (86.4%)	584 (84.6%)	
Unmarried	13 (0.3%)	9 (0.3%)	4 (0.6%)	
Location, n(%)				0.018
City	1053 (24.9%)	856 (24.2%)	197 (28.6%)	
Village	3174 (75.1%)	2681 (75.8%)	493 (71.4%)	
Smoking, n(%)				0.485
No	3960 (93.7%)	3309 (93.6%)	651 (94.3%)	
Yes	267 (6.3%)	228 (6.4%)	39 (5.7%)	
Drinking, n(%)				0.360
Drink but less than once a month	280 (6.6%)	230 (6.5%)	50 (7.2%)	
Drink more than once a month	613 (14.5%)	524 (14.8%)	89 (12.9%)	
None of these	3334 (78.9%)	2783 (78.7%)	551 (79.9%)	
Sleep, hours	6.2 ± 2.0	6.2 ± 2.0	6.3 ± 1.9	0.095
BMI, n(%)				0.069
Underweight	205 (4.8%)	160 (4.5%)	45 (6.5%)	
Normal	1942 (45.9%)	1625 (45.9%)	317 (45.9%)	
Overweight	1474 (34.9%)	1252 (35.4%)	222 (32.2%)	
Obese	606 (14.3%)	500 (14.1%)	106 (15.4%)	
Diabetes, n(%)				0.729
No	3680 (87.1%)	3076 (87.0%)	604 (87.5%)	
Yes	547 (12.9%)	461 (13.0%)	86 (12.5%)	
Hypertension, n(%)				0.535
No	2663 (63.0%)	2236 (63.2%)	427 (61.9%)	
Yes	1564 (37.0%)	1301 (36.8%)	263 (38.1%)	
Stomach or other digestive disease, n(%)				0.002
No	2850 (67.4%)	2349 (66.4%)	501 (72.6%)	
Yes	1377 (32.6%)	1188 (33.6%)	189 (27.4%)	

Table 2 Baseline characteristics of participants after PSM

Characteristic	Overall *N* = 1380	Famine exposed *N* = 690	Famine unexposed *N* = 690	*p*-value
Age, years	62.8 ± 5.4	63.2 ± 5.2	62.5 ± 5.6	0.015
Gender, n(%)				0.005
Female	1142 (82.8%)	551 (79.9%)	591 (85.7%)	
Male	238 (17.2%)	139 (20.1%)	99 (14.3%)	
Education, n(%)				0.470
College completed or above	5 (0.4%)	3 (0.4%)	2 (0.3%)	
High school	1090 (79.0%)	536 (77.7%)	554 (80.3%)	
Less than high school	285 (20.7%)	151 (21.9%)	134 (19.4%)	
Marital status, n(%)				0.618
Divorced	192 (13.9%)	90 (13.0%)	102 (14.8%)	
Married	1179 (85.4%)	595 (86.2%)	584 (84.6%)	
Unmarried	9 (0.7%)	5 (0.7%)	4 (0.6%)	
Location, n(%)				0.953
City	396 (28.7%)	199 (28.8%)	197 (28.6%)	
Village	984 (71.3%)	491 (71.2%)	493 (71.4%)	
Smoking, n(%)				0.733
No	1298 (94.1%)	647 (93.8%)	651 (94.3%)	
Yes	82 (5.9%)	43 (6.2%)	39 (5.7%)	
Drinking, n(%)				0.106
Drink but less than once a month	116 (8.4%)	66 (9.6%)	50 (7.2%)	
Drink more than once a month	194 (14.1%)	105 (15.2%)	89 (12.9%)	
None of these	1070 (77.5%)	519 (75.2%)	551 (79.9%)	
Sleep, hours	6.3 ± 2.0	6.2 ± 2.1	6.3 ± 1.9	0.255
BMI, n(%)				0.977
Underweight	89 (6.4%)	44 (6.4%)	45 (6.5%)	
Normal	632 (45.8%)	315 (45.7%)	317 (45.9%)	
Overweight	451 (32.7%)	229 (33.2%)	222 (32.2%)	
Obese	208 (15.1%)	102 (14.8%)	106 (15.4%)	
Diabetes, n(%)				0.384
No	1196 (86.7%)	592 (85.8%)	604 (87.5%)	
Yes	184 (13.3%)	98 (14.2%)	86 (12.5%)	
Hypertension, n(%)				0.116
No	883 (64.0%)	456 (66.1%)	427 (61.9%)	
Yes	497 (36.0%)	234 (33.9%)	263 (38.1%)	
Stomach or other digestive disease, n(%)				0.006
No	954 (69.1%)	453 (65.7%)	501 (72.6%)	
Yes	426 (30.9%)	237 (34.3%)	189 (27.4%)	

the post-matching subgroup analysis were similar (Supplementary Fig. 1).

Machine learning and feature importance

The XGBoost machine learning algorithm showed good performance in predicting gastrointestinal diseases. The feature importance ranking based on SHAP values indicated that, in the unmatched data, childhood famine was the fourth most important predictive factor among all variables (Fig. 3b, d). In the matched data, the importance of childhood famine rose to second, just below sleep duration (Supplementary Fig. 2b, d). This change suggests that after controlling for confounding factors, the independent predictive power of childhood

Table 3 Multivariable logistic regression analysis of childhood famine exposure and gastrointestinal diseases

Famine	OR (95% CI) [*P*-value]		
	Model 1	**Model 2**	**Model 3**
Famine unexposed	Reference		
Famine exposed	1.34 (1.12, 1.61) [$p = 0.002$]	1.37 (1.14, 1.65) [$p < 0.001$]	1.36 (1.13, 1.63) [$p = 0.001$]

Model 1: unadjusted

Model 2: adjusted for age, gender, education, location and marital status

Model 3: adjusted for all covariates

Table 4 PSM analysis of childhood famine exposure and gastrointestinal diseases in old individuals

Analysis Period	Famine	OR (95% CI)	*P*-value
Before Matching ($N = 4,227$)	Famine unexposed	Reference	-
	Famine exposed	1.34 (1.12, 1.61)	0.002
After Matching ($N = 1,380$)	Famine unexposed	Reference	-
	Famine exposed	1.39 (1.10, 1.75)	0.005

famine for disease was more pronounced. SHAP dependency plots (Fig. 3a, c) (Supplementary Fig. 2a, c) clearly revealed that the exposed group was associated with higher SHAP values, which corroborated the logistic regression results.

Discussion

This study combines traditional epidemiological approaches with cutting-edge machine learning techniques to robustly demonstrate a significant association between childhood famine exposure and an increased risk of gastrointestinal diseases later in life. On the basis of the nationally representative CHARLS cohort, we observed that individuals exposed to famine during childhood had an approximately 34% higher risk of gastrointestinal disease (OR = 1.34, 95% CI: 1.12–1.61, p = 0.002). This effect remained robust after PSM and was

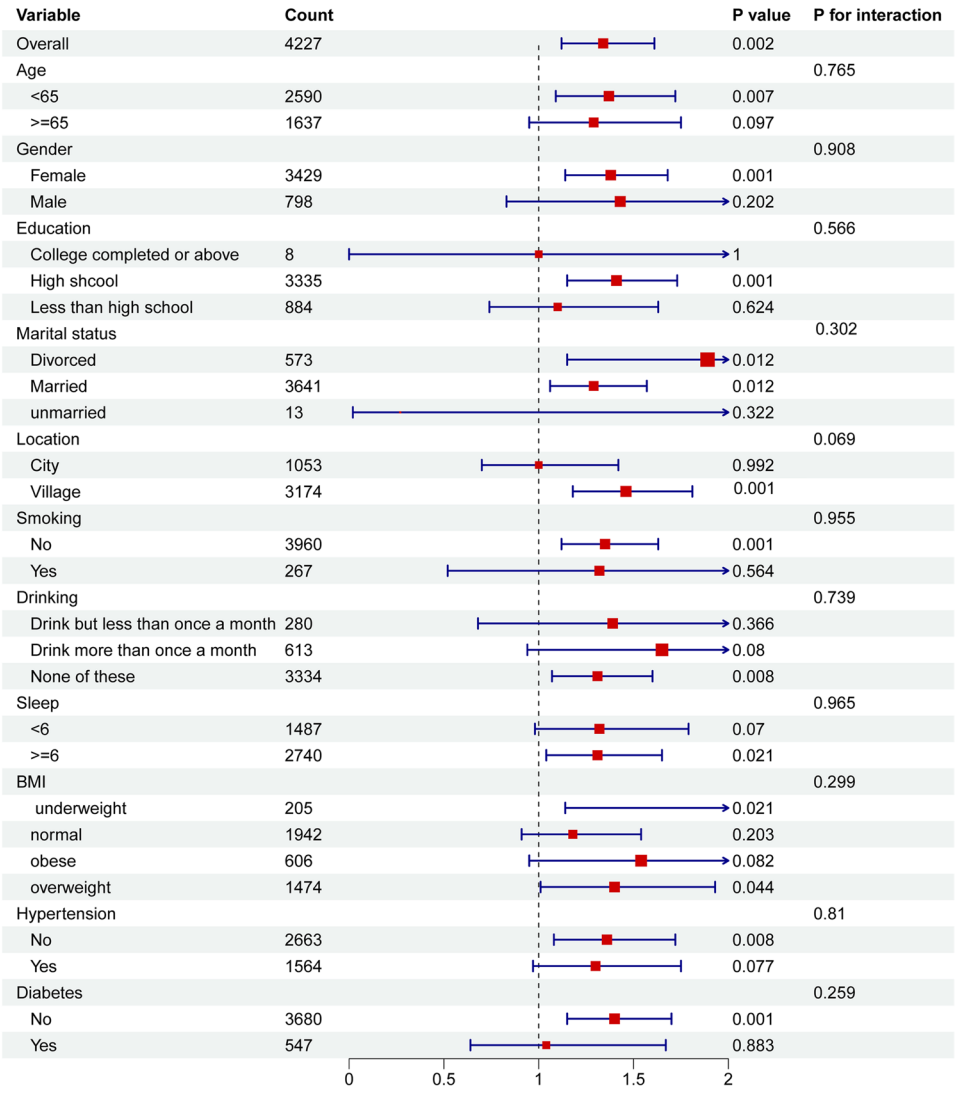

Fig. 2 Association between childhood famine exposure and gastrointestinal diseases in old individuals according to subgroup analysis

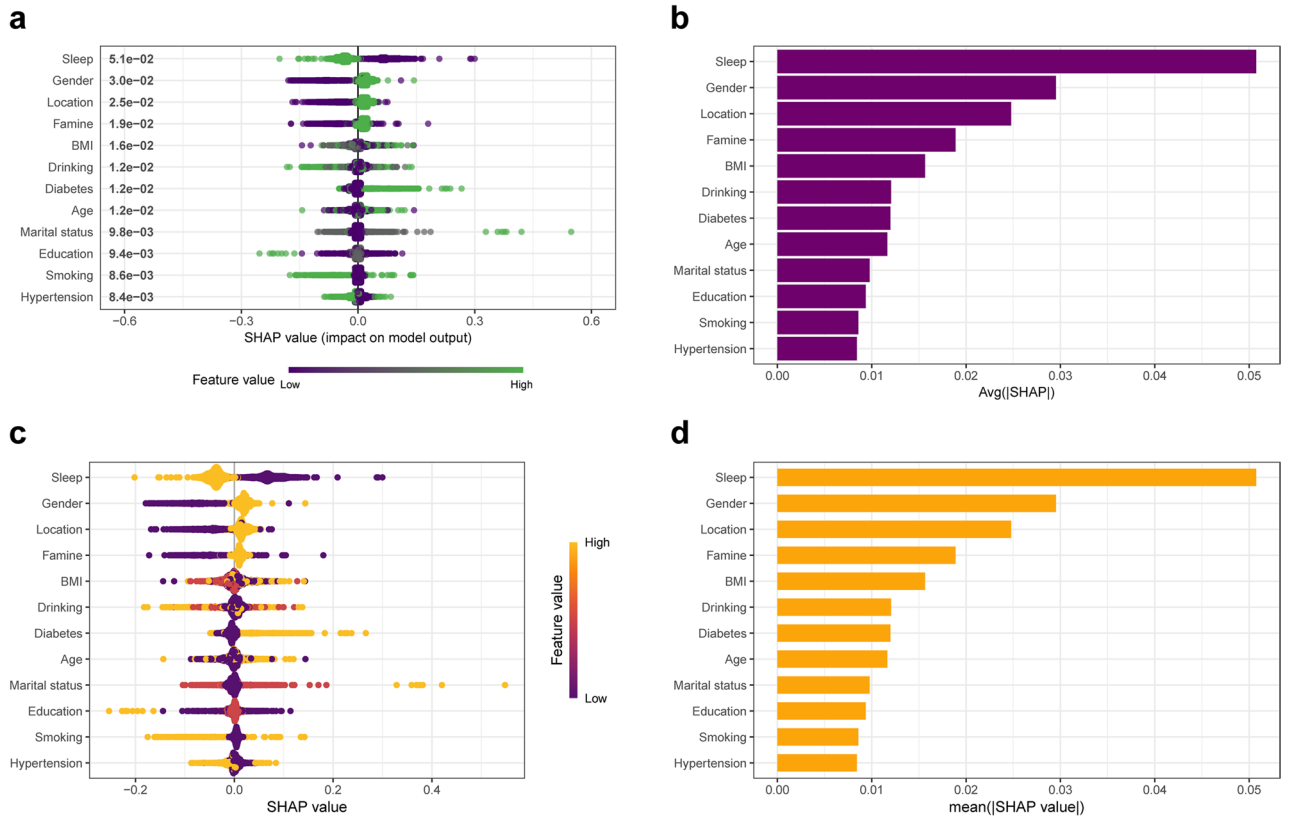

Fig. 3 The SHAP model explains the importance of variables. **a**, **b** uses the 'SHAPforxgboost' package, and (**c**, **d**) uses the 'shapviz' package to depict the importance and SHAP summary of variables in the XGBoost machine learning algorithm

identified as a key predictor of gastrointestinal disease occurrence in the XGBoost machine learning algorithm. SHAP value analysis further quantified the independent influence of famine exposure; in the matched data, its importance ranked second, only after sleep duration, underscoring the central role of early nutritional stress in the development of gastrointestinal disease later in life. The association between famine exposure and gastrointestinal diseases in old age did not significantly differ between early childhood and adolescence. Subgroup analyses confirmed the generalizability of this association, with interaction tests showing no significant heterogeneity (all P values for interaction > 0.05), indicating that the increased gastrointestinal disease risk associated with famine exposure is highly consistent across demographic, lifestyle, and chronic disease subgroups. Our findings align closely with the DOHaD paradigm and with a substantial body of empirical work linking early-life nutritional adversity to adult metabolic dysregulation, cardiovascular pathology, and susceptibility to neurodegenerative diseases [13–15]. Most prior famine studies have focused on fetal exposure, which may represent a more critical developmental window than postnatal childhood [20]. Studies of the Dutch Hunger Winter and Ukrainian famine found no consistent increase in disease risk for childhood-exposed cohorts [21, 22]. We focused on childhood because self-reported famine in CHARLS specifically capture this period; fetal exposure could not be reliably ascertained with available variables. Meanwhile, prior studies on China's large famine exposure have largely focused on dyslipidemia, osteoporosis, and functional capacity, with relatively limited exploration of long-term impacts on the digestive system [23–25]. This study is the first to quantify the relative contribution of famine exposure to digestive system diseases via a combination of PSM and the XGBoost machine learning algorithm.

The association between childhood famine exposure and gastrointestinal disease in elderly individuals may be mediated by multiple biological pathways. First, developmental programming likely leads to aberrant differentiation of intestinal epithelial cells, villous atrophy, and downregulation of digestive enzyme expression, thereby impairing nutrient absorption and barrier integrity [26, 27]. Second, epigenetic modifications—such as DNA methylation, histone acetylation, and noncoding RNA regulation—may result in persistent silencing of genes related to inflammatory mediators (e.g., IL-6 and TNF-α) and immune homeostasis, promoting chronic low-grade inflammation and increased gut permeability [28–30].

Third, gut microbiota dysbiosis represents a critical intermediary; early nutrient deprivation may disrupt colonization by beneficial taxa, foster the growth of conditionally pathogenic microbes, and create a proinflammatory milieu, which, via the gut–brain axis and gut–liver axis, can amplify systemic metabolic disturbances [31–33]. Finally, the "two-hit" model posits that early famine acts as the first hit, inducing latent vulnerability, whereas late-life oxidative stress, hormonal dysregulation, or environmental toxin exposure constitutes a second hit that triggers clinical phenotypes [26, 34].

This study provides empirical support for the DOHaD hypothesis within the field of gastroenterology, reinforcing the notion that early environmental exposures have lasting effects on lifelong health. In addition, identifying a history of childhood famine exposure could facilitate the inclusion of such individuals in high-risk screening cohorts for elderly individuals with gastrointestinal disease, with recommendations for routine assessment of intestinal permeability markers and microbiome diversity. Interventions for famine survivors should emphasize nutritional supplementation, probiotic modulation, and lifestyle optimization to mitigate potential epigenetic imprinting and reduce disease burden. Such strategies have the potential to promote health and conserve healthcare resources.

Limitations.

This study has several limitations. First, the broad outcome definition of gastrointestinal diseases encompasses heterogeneous conditions, potentially underestimating subtype-specific associations. Future studies with clinical diagnoses would be valuable. Second, recall bias for both exposure and outcome (self-reported) remain possible. Third, methodologically rigorous famine studies require careful consideration of age differences, cohort effects, and survival bias [35, 36]. We addressed confounding through multivariable adjustment and PSM, though residual sex and age imbalance after matching may introduce minor bias. Fourth, establishing dose–response relationships are crucial in famine research. Emerging literature has developed famine severity indices using excess mortality or grain procurement data [36, 37]. Unfortunately, CHARLS lacks individual-level severity measures or childhood province data during famine, preventing direct incorporation; current city/village residence may not reflect childhood exposure location. Future research should incorporate objective biomarkers and explore intergenerational transmission to further elucidate the underlying mechanisms involved.

Conclusions

Childhood famine exposure represents a significant risk factor for gastrointestinal diseases in old individuals. Incorporating this simple yet powerful indicator into routine geriatric assessments could facilitate early identification of high-risk individuals and enable targeted interventions to mitigate this long-term health burden.

Abbreviations

DOHaD	Developmental Origins of Health and Disease
CHARLS	China Health and Retirement Longitudinal Study
SD	Standard deviation
PSM	Propensity score matching
SHAP	SHapley Additive exPlanations

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-026-26461-x.

Supplementary Material 1.

Authors' contributions

All the authors devised the study. Qingquan Yang completed the data collection. Zhiyuan Rong completed the statistical analysis. All the authors made the table and figure. Zhiyuan Rong conceptualized the initial manuscript collectively. Qingquan Yang edited the manuscript and provided revisions. All the authors have read and approved the final version of the manuscript.

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Data availability

The data are available online on the website of the CHARLS (http://charls.pku.edu.cn/).

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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