Individual and Combined Effect of Famine Exposure and Obesity Parameters on Dyslipidemia in Mid-Aged and Older Adult: A Population-Based Cross-Sectional Study

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Abstract

Background: Undernutrition in early life may have a lifelong effect on adult health. The associations between undernutrition and obesity parameters and dyslipidemia were inconsistent. The present study aimed to investigate the individual and combined effects of famine exposure and obesity parameters on dyslipidemia in middle-aged and older Chinese.

Method: Data were selected from the China Health and Retirement Longitudinal Study Wave2011. The analytic sample included 9427 subjects aged 45 to 90. The present study analyzed data from 9427 middle-aged and older Chinese selected from the China Health and Retirement Longitudinal Study (CHARLS Wave2011). Differences between baseline characteristics and famine exposure/BMI levels/WC levels were evaluated using the Chi-square test, t-test, and F-test. Then, the difference in the prevalence of dyslipidemia between characteristic groups was also estimated by the Chi-square and t-test. Finally, multivariable-adjusted logistic regression models examined associations of famine exposure and obesity parameters with odds of prevalence of dyslipidemia.

Results: Among the 9427 participants, 1097(11.64%) participants had been exposed to the Chinese famine during the fetal stage, whereas 3763(39.92%) participants and 3251(34.49%) participants had been exposed to the famine during childhood and adolescence/adult stage, respectively. Regarding the participants with BMI measurements, 2771(29.39%) were overweight and 1105(11.72%) were obese, whereas 3955(41.95%) of the participants with WC measurements were obese, respectively. Furthermore, 1899(43.23%) reported having dyslipidemia in males and 1860(36.95%) in females. In multivariable-adjusted model, famine exposure and obesity parameters were associated with prevalence of dyslipidemia independently in total populations[(1) Model three^c, famine exposure with prevalence of dyslipidemia: the fatal exposed vs no exposed group, 1.32 (95% CI 1.12, 1.56); childhood-exposed vs no exposed group, 1.49 (95% CI 1.30, 1.70); the adolescence/adult-exposed vs no exposed group, 1.49 (95% CI 1.30, 1.71) ; *P* for trend=0.000; (2) Model three^e, famine exposure with prevalence of dyslipidemia: the fatal exposed vs no exposed group, 1.29 (95% CI 1.09, 1.52); childhood-exposed vs no exposed group, 1.39 (95% CI 1.22, 1.59); the adolescence/adult-exposed vs no exposed group, 1.27 (95% CI 1.11, 1.46) ; *P* for trend=0.002; (3) Model three^g, BMI levels with prevalence of dyslipidemia: overweight vs normal, 2.06 (95% CI 1.86, 2.27); obesity vs normal, 2.82(95% CI 2.42, 3.27) ; *P* for trend=0.000; (4) WC levels with prevalence of dyslipidemia: overweight vs normal, 2.24 (95% CI 2.05, 2.45)]. When stratified by sex, the results in females were mostly similar to those in the total population. In a multivariable logistic regression model three^c, associations between famine exposure and dyslipidemia were not observed [fatal exposed group vs non-exposed group: 0.98 (95% CI 0.75, 1.28); childhood-exposed group vs non-exposed group: 0.96 (95% CI 0.78, 1.19); adolescence/adult exposed group vs non-exposed group: 0.86 (95% CI 0.69, 1.07)] independently of BMI only (*P* for trend =0.110). However, in a multivariable logistic regression model three^e, associations between famine exposure and dyslipidemia in male were partly observed [fatal exposed group vs non-exposed group: 0.97 (95% CI 0.74, 1.26); childhood-exposed group vs non-exposed group: 0.91 (95% CI 0.74, 1.13); adolescence/adult exposed group vs non-exposed group: 0.73 (95% CI 0.59, 0.91)] independently of BMI only (*P* for trend =0.001). In general, the significant synergism between famine exposure and obesity parameters in lowering the prevalence of dyslipidemia was observed in males while the significant synergism in increasing prevalence of dyslipidemia was observed in females (*P*-interaction =0.000).

Conclusion: Individual and combined associations of obesity parameters and famine exposure with the prevalence of dyslipidemia were observed in middle-aged and elderly Chinese.

Background

Dyslipidemia is characterized by an elevated low-density lipoprotein cholesterol (LDL-c), and/or triglycerides (TG), and/or total cholesterol (TC), and/or decreased high-density lipoprotein cholesterol (HDL-c). It was an important risk factor for cardiovascular disease (CVD), representing 31%[1] of all global deaths. The prevalence of dyslipidemia was 34%[2] among Chinese adults aged greater than 18-years-old, and was 43%[3] among Chinese people aged 40 to 100 years. However, the rates of awareness, treatment, and control were 31.0%, 19.5%, and 8.9%, respectively. The prevalence of dyslipidemia among Chinese adults was high but awareness, treatment, and control of dyslipidemia were still low. Dyslipidemia is a serious public health problem and causes a serious burden to families and society. Therefore, it emphasizes the effective, practical, and sustainable promotion of prevention and treatment strategies to prevent dyslipidemia risk factors[4–6]. Though the etiology of dyslipidemia is complex, it was known as one of the strongest risk factors was overweight/obesity. Thus, increased body mass index (BMI) or centrally located body fat (especially waist circle [WC]) increases the risk of developing dyslipidemia. In addition to known and probable risk factors for dyslipidemia, early life mal-nutrition may also affect dyslipidemia.

It was hypothesized that early developmental adaption in response to malnutrition in early life, which are key determinants of short-term survival, have adverse metabolic outcomes[7–9]. Historical famine exposure has provided a unique and natural opportunity to test the hypothesis. From 1959–1961, China suffered from extreme food shortages. It was one of the most famine disasters in human history, 15–43 million people died. We selected participants from the age group for our study to understand the impact of malnutrition in early life on their health. Though some studies have indicated malnutrition in early life is relationship with the risk of developing chronic diseases in adult(e.g. type 2 diabetes[10], metabolic syndrome[11, 12], cardiovascular disease, hypertension[13, 14], and cognitive decline[15, 16]). Several famine studies[17–19] also have provided evidences to support the association between famine exposure and increased risk of dyslipidemia. However, it is not completely understood association and interaction analysis between famine exposure and obesity parameter and dyslipidemia in the older adult.

Therefore, in present study, we use the data derived from the China Health and Retirement Longitudinal Study (CHARLS) Wave1 to investigate the individual and combined effects of famine exposure and obesity parameter (BMI and WC) on dyslipidemia after adjustment for confounding variables.

Methods

Study design and setting

Data from the China Health and Retirement Longitudinal Study (CHARLS) Wave1 were used in our research.

The CHARLS was a nationally representative longitudinal study conducted by the China Centre for Economic Research at Peking University[20] from 2011. In the 2011 CHARLS Wave1, at baseline, 13107 individuals were recruited for a longitudinal study, after excluding participants who had missing values of the baseline characteristics and measurements, 9427 were included in the study. All data are openly published as microdata at <http://charls.pku.edu.cn/index/zh-cn.html> with no direct contact with all participants. The Ethics Committee of the China Centre for Economic Research at Peking University approved this study, all participants have provided the informed consent before the data collection.

Subjects

The subjects of the study were selected from the China Health and Retirement Longitudinal Study (CHARLS), Wave 1 (2011) [20]. The age of CHARLS involved 9427 individuals were [mean $\pm$ standard deviation age = 59.51 $\pm$ 9.32 years, ranged from 45 to 90 years]. The mean and standard deviation of age were 60.26 $\pm$ 9.23 years (ranged from 45 to 90 years) in males and 58.85 $\pm$ 9.35 years (ranged from 45 to 96 years) in females.

Baseline Characteristics

Baseline variables including age, sex(0 = male, 1 = female), educational levels (0 = Illiterate, 1 = Less than elementary school, 2 = High school, 3 = Above vocational school), marital status(0 = Single, 1 = Married), place of residence(0 = Rural, 1 = Urban), smoking habits(0 = No, 1 = Former smoke, 2 = Current smoke), alcohol consumption (0 = No, 1 = Less than once a month, 2 = More than once a month), eating meals (0 = $\leq$ 2 meals per day, 1 = 3 meals per day, 2 = $\geq$ 4 meals per day), social and leisure activities (0 = No, 1 = Yes), experience of a traumatic event(0 = No, 1 = Yes), physical exercise habit(0 = No, 1 = Less than regular physical exercises, 2 = Regular physical exercises) were collected using a type of self-report method. Most variables were depending on our previous research studies[21–26].

Measurements

BMI was calculated based on the measured weight and height of the participants. Tapeline was localized at navel levels to read the waist circle (WC) at the end of exhalation. Using the standard China definition, BMI was categorized into three groups[27]: underweight and normal (BMI < 24 kg/m²), overweight (24 $\leq$ BMI < 28 kg/m²), and obesity (BMI $\geq$ 28 kg/m²). Central obesity was defined as a WC[28] of $\geq$ 90 cm for men and $\geq$ 85 cm for women. Frozen plasma LDL-c, HDL-c, TG, and total TC from venous blood samples stored frozen at -20°C were analyzed by the Youanmen Center for Clinical Laboratory at Capital Medical University using the enzymatic colormetric test. The dyslipidemia was defined based on the guidelines provided in the third report of the National Cholesterol Education Programme (NCEP) Adult Treatment Panel III (NCEP ATP III): TC $\geq$ 5.2 mmol/L; TG $\geq$ 1.7 mmol/L; HDL-C < 1.0 mmol/L in male and < 1.3 mmol/L in female; LDL-C $\geq$ 3.4 mmol/L[29].

Exposure Age And Exposed Stages

Famine exposure is set up on the birth year. Like the previous Chinese famine study[30], participants were categorized into four exposure cohorts: no-exposed stage (born between 1963/01/01 and 1966/12/31), fetal exposed stage (born between 1959/01/01 and 1962/12/31), childhood exposed stage (born between 1949/01/01 and 1958/12/31), adolescence/adult exposed stage (born between 1921/01/01 and 1948/12/31).

Statistical analysis

The data are presented as means and standard deviation (SD) unless indicated otherwise. Means and standard deviation (continuous data) were used to describe continuous variable (age), and number and percentage (categorical data) were used to assess the categorical variables (sex, educational levels, marital status, residence places, alcohol drinking, smoking habit, eating meals, social and leisure activities, the experience of a traumatic event, taking physical activity or exercise, famine exposure, BMI categories, WC categories, and dyslipidemia categories). Between-group differences according to dyslipidemia (dyslipidemia, no-dyslipidemia) were evaluated by the chi-square test (categorical data). Differences between baseline characteristics (marital status, residence places, social and leisure activities, the experience of a traumatic event, taking physical activity or exercise) and categories of famine exposure stages/BMI/WC were also evaluated using the chi-square test (categorical data). Age between groups was used by t-test or F-test. For the present study, logistic regression models were used to compute ORs with accompanying 95% CIs as estimates of associations of BMI/WC categories and exposure stages separately and in combination, with the prevalence of dyslipidemia. Analyses were performed using SPSS software, version 25.0 (IBM SPSS, Armonk, NY, USA), with a 5% significance level.

Results

Table 1 shows the basic characteristics of participants. A total of 9427 individuals were enrolled into the study, 4393(46.60%) participants and 5034(53.40%) participants were male and female, respectively. Among males, 461(10.49%) participants had been exposed to the Chinese famine during the fetal stage, whereas 1766(40.20%) participants and 1662(37.83%) participants had been exposed to the famine during childhood and adolescence/adult stage, respectively. Among females, 636(12.63%) participants had been exposed to the Chinese famine during the fetal stage, whereas 1997(35.70%) participants and 1589(31.57%) participants had been exposed to the famine during childhood and adolescence/adult stage, respectively. The distribution of history of accidental injury did not demonstrate significantly statistical difference among the four birth cohorts. On the other hand, the difference was observed in the

distribution of age, sex, educational levels, place of residence, marital status, cigarette smoking, alcohol habit, eating habit, social events, and physical exercises habit. Regarding the males, 2879(65.95%) were underweight and normal, 1127(25.65%) were overweight and 369(8.40%) were obese, whereas 2654(52.72%), 1644(32.66%) and 736(14.62%) of the females were underweight and normal, overweight, and obese, respectively. Furthermore, significant differences in distribution were observed between BMI levels in all of the variables, including age, sex, educational levels, marital status, place of residence, cigarette smoking, alcohol habit, eating habit, social events, and physical exercises habit, except for history of accidental injury. Among the WC measures, 1316(29.96%) were central obesity in males and 2639(52.42%) in females. The proportions on the characteristics were statistically different between the WC groups except for marital status.

Table 1
Characteristics of participants in the cohort study by level of famine exposure, BMI, and central obesity

Characteristics	Famine exposure					BMI				
	No-exposed	Fetal exposed	Childhood-exposed	Adolescence/ adult-exposed	χ^2/F	<i>P</i>	Normal	Overweight	Obesity	χ^2/F
N	1316	1097	3763	3251			5551	2771	1105	
Age	46.75 ± 1.08	50.27 ± 1.17	57.57 ± 2.78	70.02 ± 5.71	15498.488	0.000	60.66 ± 9.60	58.10 ± 8.73	57.26 ± 8.40	108
Gender										
male	504(38.30)	461(42.02)	1766(46.93)	1662(51.12)	72.572	0.000	2897(52.19)	1127(40.67)	369(33.39)	186
female	812(61.70)	636(57.98)	1997(53.07)	1589(48.88)			2654(47.81)	1644(59.33)	736(66.61)	
Education										
Illiterate	147(11.17)	192(17.5)	1090(28.97)	1284(39.50)	792.449	0.000	1696(30.55)	718(25.91)	299(27.06)	46.
Less than elementary school	993(75.46)	665(60.62)	2336(62.08)	1793(55.15)			3388(61.03)	1717(61.96)	682(61.72)	
High school	124(9.42)	204(18.60)	255(6.78)	44(1.35)			326(5.87)	217(7.83)	84(7.60)	
Above vocational school	52(3.95)	36(3.28)	82(2.18)	130(4.00)			141(2.54)	119(4.29)	40(3.62)	
Marital status										
Single	48(3.65)	55(5.01)	303(8.05)	762(23.44)	578.51	0.000	813(14.65)	251(9.06)	104(9.41)	63.
Married	1268(96.35)	1042(94.99)	3460(91.95)	2489(76.56)			4738(85.35)	2520(90.94)	1001(90.59)	
Place of residence										
Rural	824(62.61)	706(64.36)	2413(64.12)	2165(66.59)	8.195	0.042	3894(70.15)	1617(58.35)	597(54.03)	176
Urban	492(37.39)	391(35.64)	1350(35.88)	1086(33.41)			1657(29.85)	1154(41.65)	508(45.97)	
Cigarette smoking										
NO	914(69.45)	700(63.81)	2239(59.5)	1854(57.03)	123.017	0.000	3042(54.8)	1856(66.98)	809(73.21)	26.
Former smoke	70(5.32)	57(5.20)	321(8.53)	406(12.49)			472(8.5)	279(10.07)	103(9.32)	
Current smoke	332(25.23)	340(30.99)	1203(31.97)	991(30.48)			2037(36.7)	636(22.95)	193(17.47)	
Alcohol habit										
NO	880(66.87)	712(64.9)	2487(66.09)	2262(69.58)	24.565	0.000	3565(64.22)	1944(70.16)	832(75.29)	73.
Less than once a month	117(8.89)	110(10.03)	306(8.13)	207(6.37)			448(8.07)	209(7.54)	83(7.51)	
More than once a month	319(24.24)	275(25.07)	970(25.78)	782(24.05)			1538(27.71)	618(22.30)	190(17.19)	
Eating habit										
≤ 2 meals per day	193(14.67)	149(13.58)	439(11.67)	465(14.3)	22.098	0.001	837(15.08)	298(10.75)	111(10.05)	57.
3 meals per day	1113(84.57)	938(85.51)	3259(86.61)	2744(84.4)			4620(83.23)	2445(88.24)	989(89.50)	
≥ 4 meals per day	10(0.76)	10(0.91)	65(1.73)	42(1.29)			94(1.69)	28(1.01)	5(0.45)	
Social events										
No	565(42.93)	465(42.39)	1906(50.65)	1732(53.28)	65.433	0.000	2925(52.69)	1269(45.80)	474(42.90)	57.
Yes	751(57.07)	632(57.61)	1857(49.35)	1519(46.72)			2626(47.31)	1502(54.20)	631(57.10)	
History of accidental injury										

Characteristics	Famine exposure						BMI			
	No-exposed	Fetal exposed	Childhood-exposed	Adolescence/ adult-exposed	χ^2/F	<i>P</i>	Normal	Overweight	Obesity	χ^2/F
No	1191(90.5)	986(89.88)	3381(89.85)	2949(90.71)	1.734	0.629	4991(89.91)	2497(90.11)	1019(92.22)	5.6
Yes	125(9.5)	111(10.12)	382(10.15)	302(9.29)			560(10.09)	274(9.89)	86(7.78)	
Physical exercises habit										
No physical exercise	794(60.33)	644(58.71)	2286(60.75)	2080(63.98)	16.153	0.013	3451(62.17)	1658(59.83)	695(62.90)	14.
Less than regular physical exercises	258(19.6)	234(21.33)	744(19.77)	561(17.26)			1081(19.47)	536(19.34)	180(16.29)	
Regular physical exercises	264(20.06)	219(19.96)	733(19.48)	610(18.76)			1019(18.36)	577(20.82)	230(20.81)	

Table 2 shows the characteristics of study participants categorized by dyslipidemia. Of the participants, 1899(43.23%) reported having dyslipidemia in male and 1860(36.95%) in the female. Significant differences were observed in sex, place of residence, cigarette smoking, alcohol habit, social events, famine exposure, BMI levels, and WC groups ($P < 0.05$) between participants with and without dyslipidemia.

Table 2
Characteristics of study participants of cross-sectional study categorized by dyslipidemia (N = 9427)

Variables	Without dyslipidemia N = 3759	Dyslipidemia N = 5668	Total	χ^2/t	P
Age	59.38 ± 9.52	59.59 ± 9.19	59.51 ± 9.32	-1.085	0.278
Gender					
male	1899(50.52)	2494(44.00)	4393(46.60)	38.578	0.035
female	1860(49.48)	3174(56.00)	5034(53.40)		
Education					
Illiterate	1041(27.69)	1672(29.50)	2713(28.78)	4.584	0.205
Less than elementary school	2356(62.68)	3431(60.53)	5787(61.39)		
High school	243(6.46)	384(6.77)	627(6.65)		
Above vocational school	119(3.17)	181(3.19)	300(3.18)		
Marital status					
Single	452(12.02)	716(12.63)	1168(12.39)	0.769	0.38
Married	3307(87.98)	4952(87.37)	8259(87.61)		
Place of residence					
Rural	2562(68.16)	3546(62.56)	6108(64.79)	31.011	0.000
Urban	1197(31.84)	2122(37.44)	3319(35.21)		
Cigarette smoking					
NO	2177(57.91)	3530(62.28)	5707(60.54)	42.537	0.000
Former smoke	301(8.01)	553(9.76)	854(9.06)		
Current smoke	1281(34.08)	1585(27.96)	2866(30.40)		
Alcohol habit					
NO	2453(65.26)	3888(68.60)	6341(67.26)	11.897	0.003
Less than once a month	321(8.54)	419(7.39)	740(7.85)		
More than once a month	985(26.2)	1361(24.01)	2346(24.89)		
Eating habit					
≤ 2 meals per day	527(14.02)	719(12.69)	1246(13.22)	3.51	0.173
3 meals per day	3182(84.65)	4872(85.96)	8054(85.44)		
≥ 4 meals per day	50(1.33)	77(1.36)	127(1.35)		
Social events					
No	1965(52.27)	2703(47.69)	4668(49.52)	19.013	0.000
Yes	1794(47.73)	2965(52.31)	4759(50.48)		
History of accidental injury					
No	3398(90.4)	5109(90.14)	8507(90.24)	0.172	0.678
Yes	361(9.6)	559(9.86)	920(9.76)		
Physical exercises habit					
No physical exercise	2266(60.28)	3538(62.42)	5804(61.57)	5.775	0.056
Less than regular physical exercises	758(20.16)	1039(18.33)	1797(19.06)		
Regular physical exercises	735(19.55)	1091(19.25)	1826(19.37)		
Famine exposure					
No-exposed	594(15.80)	722(12.74)	1316(13.96)	20.7044	0.000

BMI: body mass index.

Variables	Without dyslipidemia N = 3759	Dyslipidemia N = 5668	Total	χ^2/t	P
Fetal exposed	432(11.49)	665(11.73)	1097(11.64)		
Childhood-exposed	1431(38.07)	2332(41.14)	3763(39.92)		
Adolescence/adult-exposed	1302(34.64)	1949(34.39)	3251(34.49)		
BMI					
Normal	2644(70.34)	2907(51.29)	5551(58.88)	352.436	0.000
Overweight	848(22.56)	1923(33.93)	2771(29.39)		
Obesity	267(7.1)	838(14.78)	1105(11.72)		
Central obesity					
Normal	2632(70.02)	2840(50.11)	5472(58.05)	367.999	0.000
Obesity	1127(29.98)	2828(49.89)	3955(41.95)		
BMI: body mass index.					

Table 3 shows the separate associations of famine exposure, BMI and central obesity with the prevalence of dyslipidemia. Firstly, after controlling for confounding factors including age, educational levels, marital status, place of residence, smoking habits, drinking habits, eating meals, social and leisure activities, the experience of a traumatic event, taking physical activity or exercise, and famine exposure in a multivariable logistic regression model three, higher odds of prevalence of dyslipidemia in the total population were observed with increasing levels of BMI [overweight vs normal: 2.06 (95% CI 1.86, 2.27); obesity vs normal: 2.82(95% CI 2.42, 3.27)] and WC [overweight vs normal: 2.24(95% CI 2.05, 2.45)] independently of famine stages only (BMI, P for trend = 0.000). When stratified by sex, the results of model three in both males and females were mostly similar to those in the total population. Secondly, after controlling for confounding factors including age, educational levels, marital status, place of residence, smoking habits, drinking habits, eating meals, social and leisure activities, the experience of a traumatic event, taking physical activity or exercise, and BMI in a multivariable logistic regression model three, higher odds of prevalence of dyslipidemia in the total population were observed with famine exposed stages [fatal exposed group vs non-exposed group: 1.32 (95% CI 1.12, 1.56); childhood-exposed group vs non-exposed group: 1.49 (95% CI 1.30, 1.70); adolescence/adult exposed group vs non-exposed group: 1.49 (95% CI 1.30, 1.71)] independently of BMI only (P for trend = 0.000). When stratified by sex, the results of model three in females were mostly similar to those in the total population. However, after controlling for confounding factors including age, educational levels, marital status, place of residence, smoking habits, drinking habits, eating meals, social and leisure activities, the experience of a traumatic event, taking physical activity or exercise, and BMI in a multivariable logistic regression model three, associations between famine exposure and dyslipidemia were not observed [fatal exposed group vs non-exposed group: 0.98 (95% CI 0.75, 1.28); childhood-exposed group vs non-exposed group: 0.96 (95% CI 0.78, 1.19); adolescence/adult exposed group vs non-exposed group: 0.86 (95% CI 0.69, 1.07)] independently of BMI only (P for trend = 0.110). Lastly, after controlling for confounding factors including age, educational levels, marital status, place of residence, smoking habits, drinking habits, eating meals, social and leisure activities, the experience of a traumatic event, taking physical activity or exercise, and WC in a multivariable logistic regression model three, higher odds of prevalence of dyslipidemia in the total population were observed with famine exposed stages [fatal exposed group vs non-exposed group: 1.25 (95% CI 1.06, 1.47); childhood-exposed group vs non-exposed group: 1.52 (95% CI 1.34, 1.73); adolescence/adult exposed group vs non-exposed group: 2.66 (95% CI 2.33, 3.03), P for trend = 0.000] independently of WC only (P for trend = 0.000). When stratified by sex, the results of model three in females were mostly similar to those in the total population. Furthermore, after controlling for confounding factors including age, educational levels, marital status, place of residence, smoking habits, drinking habits, eating meals, social and leisure activities, the experience of a traumatic event, taking physical activity or exercise, and WC in a multivariable logistic regression model three, associations between famine exposure and dyslipidemia in male were partly observed [fatal exposed group vs non-exposed group: 0.97 (95% CI 0.74, 1.26); childhood-exposed group vs non-exposed group: 0.91 (95% CI 0.74, 1.13); adolescence/adult exposed group vs non-exposed group: 0.73 (95% CI 0.59, 0.91)] independently of BMI only (P for trend = 0.001).

Table 3
Separate associations of famine exposure, BMI, and central obesity with prevalence of dyslipidemia (N = 9427)

Variables	Male (OR and 95% CI for dyslipidemia)			Female (OR and 95% CI for dyslipidemia)			Total (OR and 95% CI for dyslipidemia)	
Famine exposure	Model one ^a	Model two ^b	Model three ^c	Model one ^a	Model two ^b	Model three ^c	Model one ^a	Model two ^b
No-exposed	1.00(reference)	1.00(reference)	1.00(reference)	1.00(reference)	1.00(reference)	1.00(reference)	1.00(reference)	1.00(reference)
Fetal exposed	0.92(0.71,1.19)	0.97(0.74,1.27)	0.98(0.75,1.28)	1.54(1.25,1.90)	1.56(1.26,1.93)	1.55(1.25,1.92)	1.27(1.08,1.49)	1.30(1.10,1.53)
Childhood-exposed	0.84(0.69,1.03)	0.94(0.77,1.17)	0.96(0.78,1.19)	1.86(1.58,2.20)	2.00(1.69,2.38)	1.99(1.68,2.37)	1.34(1.18,1.52)	1.40(1.22,1.60)
Adolescence/adult-exposed	0.67(0.55,0.82)	0.85(0.68,1.05)	0.86(0.69,1.07)	2.07(1.74,2.46)	2.43(2.01,2.94)	2.41(1.99,2.93)	1.23(1.08,1.40)	1.40(1.22,1.60)
<i>P</i> for trend	0.000	0.074	0.110	0.000	0.000	0.000	0.008	0.000
Famine exposure	Model two ^d		Model three ^e	Model two ^d		Model three ^e	Model one ^a	
No-exposed	1.00(reference)		1.00(reference)	1.00(reference)		1.00(reference)	1.00(reference)	
Fetal exposed	0.95(0.73,1.25)		0.97(0.74,1.26)	1.52(1.23,1.88)		1.51(1.22,1.87)	1.27(1.08,1.49)	
Childhood-exposed	0.89(0.72,1.10)		0.91(0.74,1.13)	1.86(1.56,2.20)		1.85(1.56,2.19)	1.34(1.18,1.52)	
Adolescence/adult-exposed	0.72(0.58,0.89)		0.73(0.59,0.91)	2.04(1.69,2.47)		2.04(1.69,2.47)	1.23(1.08,1.40)	
<i>P</i> for trend	0.000		0.001	0.000		0.000	0.000	
BMI	Model one ^a	Model two ^f	Model three ^g	Model one ^a	Model two ^f	Model three ^g	Model one ^a	Model two ^f
Underweight and normal	1.00(reference)	1.00(reference)	1.00(reference)	1.00(reference)	1.00(reference)	1.00(reference)	1.00(reference)	1.00(reference)
Overweight	2.51(2.17,2.91)	2.42(2.08,2.81)	2.40(2.06,2.79)	1.69(1.49,1.92)	1.79(1.57,2.04)	1.78(1.56,2.03)	2.06(1.87,2.27)	2.11(1.90,2.34)
Obesity	4.38(3.35,5.72)	4.13(3.16,5.41)	4.10(3.13,5.38)	2.13(1.78,2.55)	2.29(1.91,2.76)	2.26(1.88,2.72)	2.85(2.46,3.31)	2.90(2.48,3.39)
<i>P</i> for trend	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Central obesity	Model one ^a	Model two ^f	Model three ^g	Model one ^a	Model two ^f	Model three ^g	Model one ^a	Model two ^f
Normal	1.00(reference)	1.00(reference)	1.00(reference)	1.00(reference)	1.00(reference)	1.00(reference)	1.00(reference)	1.00(reference)
Obesity	2.89(2.51,3.33)	2.76(2.39,3.19)	2.73(2.36,3.15)	1.94(1.72,2.18)	1.89(1.68,2.12)	1.88(1.67,2.11)	2.33(2.13,2.54)	2.29(2.09,2.50)
BMI: body mass index; WC: waist circle; OR: odds ratios; CI: confidence interval.								

Table 4 shows the combined associations of obesity parameters and famine exposure with the prevalence of dyslipidemia in males, females, and the total adults. Compared with the combination of normal BMI/WC level and no-exposed famine stage, all groups trended towards higher or lower odds of prevalence of dyslipidemia. First, in multivariable model three, the greatest increase in odds was observed for the no-exposed stage and obesity combination in males (no-exposed stage and obesity in BMI: OR 9.41; 95%CI 3.65, 24.37; no-exposed stage and obesity in WC: OR 2.89; 95%CI 1.91, 4.37). Second, in multivariable model three, the greatest increase in odds was observed for the adolescence/adult exposed stage and obesity combination in females (adolescence/adult exposed stage and obesity in BMI: OR 5.81; 95%CI 3.79, 8.90; adolescence/adult exposed stage and obesity in WC: OR 3.70; 95%CI 2.87, 4.76). Third, in multivariable-adjusted model three, the highest odds of prevalence of dyslipidemia were observed for the adolescence/adult exposed stage and obesity combination in total adults (childhood-exposed stage and obesity in BMI: OR 4.18; 95%CI 3.18, 5.50; adolescence/adult exposed stage and obesity in WC: OR 2.86; 95%CI 2.38, 3.43). Finally, combined associations of obesity parameters and famine exposure with the prevalence of dyslipidemia were observed in both males and females (*P*-interaction = 0.000).

Table 4
Combined associations of obesity parameters and famine exposure with prevalence of dyslipidemia

Famine exposure	prevalence of dyslipidemia Odds ratio(95%CI)								
	Model one ^a				Model two ^b				Model three ^c
	BMI levels				BMI levels				BMI levels
Male	Normal	overweight	obesity	P for trend	Normal	overweight	obesity	P for trend	Normal
No-exposed	1.00(reference)	1.85(1.24,2.76)	9.8(3.81,25.23)	0.000	1.00(reference)	1.82(1.22,2.72)	9.5(3.69,24.46)	0.000	1.00(reference)
Fetal exposed	0.95(0.68,1.33)	2.00(1.29,3.10)	4.36(2.05,9.27)	0.000	0.95(0.68,1.33)	1.99(1.29,3.09)	4.23(1.99,9.01)	0.000	0.96(0.69,1.34)
Childhood-exposed	0.89(0.68,1.15)	2.08(1.53,2.83)	4.29(2.66,6.91)	0.000	0.88(0.68,1.15)	2.03(1.5,2.77)	4.14(2.57,6.67)	0.000	0.91(0.71,1.16)
Adolescence/adult-exposed	0.74(0.57,0.97)	2.33(1.67,3.24)	1.95(1.20,3.18)	0.000	0.74(0.57,0.96)	2.25(1.62,3.14)	1.88(1.16,3.06)	0.000	0.75(0.57,0.98)
P for trend	0.000	0.000	0.000		0.000	0.000	0.000		0.000
P interaction		0.000				0.000			
	WC levels				WC levels				WC levels
	Normal	Central obesity			Normal	Central obesity			Normal
No-exposed	1.00(reference)	3.00(1.99,4.53)			1.00(reference)	2.93(1.94,4.42)			1.00(reference)
Fetal exposed	0.97(0.71,1.33)	2.72(1.76,4.20)			0.97(0.71,1.33)	2.66(1.72,4.12)			0.98(0.72,1.34)
Childhood-exposed	0.91(0.71,1.16)	2.55(1.90,3.42)			0.91(0.71,1.16)	2.46(1.84,3.31)			0.93(0.73,1.18)
Adolescence/adult-exposed	0.73(0.57,0.94)	2.10(1.56,2.83)			0.73(0.57,0.94)	2.04(1.51,2.75)			0.74(0.57,0.97)
P for trend	0.000	0.000			0.000	0.000			0.000
P interaction	0.000				0.000				0.000
Female	Normal	overweight	obesity	P for trend	Normal	overweight	obesity	P for trend	Normal
No-exposed	1.00(reference)	1.95(1.43,2.66)	1.68(1.14,2.47)	0.000	1.00(reference)	1.95(1.43,2.65)	1.67(1.14,2.46)	0.000	1.00(reference)
Fetal exposed	1.56(1.14,2.12)	2.45(1.76,3.41)	4.04(2.49,6.54)	0.000	1.56(1.14,2.13)	2.45(1.76,3.41)	4.03(2.48,6.52)	0.000	1.55(1.13,2.11)
Childhood-exposed	1.95(1.54,2.48)	3.29(2.52,4.29)	4.73(3.37,6.64)	0.000	1.96(1.54,2.50)	3.29(2.52,4.29)	4.71(3.35,6.62)	0.000	1.96(1.54,2.50)
Adolescence/adult-exposed	2.18(1.71,2.78)	4.29(3.19,5.77)	5.91(3.88,9.01)	0.000	2.21(1.71,2.84)	4.30(3.18,5.82)	5.91(3.86,9.05)	0.000	2.20(1.70,2.82)
P for trend	0.000	0.000	0.000		0.000	0.000	0.000		0.000
P interaction		0.000				0.000			
	WC levels				WC levels				WC levels
	Normal	Central obesity			Normal	Central obesity			Normal
No-exposed	1.00(reference)	1.63(1.23,2.15)			1.00(reference)	1.63(1.23,2.15)			1.00(reference)
Fetal exposed	1.42(1.06,1.91)	2.65(1.96,3.58)			1.43(1.06,1.91)	2.65(1.97,3.58)			1.42(1.06,1.91)
Childhood-exposed	1.69(1.34,2.12)	3.29(2.60,4.16)			1.71(1.36,2.16)	3.31(2.61,4.19)			1.70(1.35,2.15)
Adolescence/adult-exposed	1.78(1.40,2.28)	3.66(2.87,4.67)			1.83(1.42,2.36)	3.72(2.89,4.79)			1.84(1.42,2.36)
P for trend	0.000	0.000			0.000	0.000			0.000
P interaction	0.000				0.000				0.000
Total	Normal	overweight	obesity	P for trend	Normal	overweight	obesity	P for trend	Normal

BMI: body mass index; WC: waist circle.

^a Unadjusted; age-adjusted by design

^b Adjusted for age, educational levels, marital status, place of residence;

^c Adjusted for age, educational levels, marital status, place of residence, smoking habits, drinking habits, eating meals, social and leisure activities, experience

Famine exposure	prevalence of dyslipidemia Odds ratio(95%CI)								
	Model one ^a				Model two ^b				Model three ^c
	BMI levels				BMI levels				BMI levels
No-exposed	1.00(reference)	1.85(1.45,2.36)	2.19(1.58,3.04)	0.000	1.00(reference)	1.85(1.45,2.36)	2.17(1.57,3.02)	0.000	1.00(reference)
Fetal exposed	1.26(1.00,1.58)	2.20(1.69,2.86)	3.91(2.62,5.84)	0.000	1.26(1.01,1.58)	2.21(1.70,2.87)	3.86(2.58,5.77)	0.000	1.26(1.00,1.58)
Childhood-exposed	1.35(1.13,1.60)	2.71(2.22,3.30)	4.37(3.33,5.75)	0.000	1.33(1.11,1.58)	2.63(2.15,3.21)	4.23(3.22,5.57)	0.000	1.35(1.13,1.60)
Adolescence/adult-exposed	1.26(1.06,1.50)	3.29(2.64,4.10)	3.78(2.76,5.18)	0.000	1.21(1.02,1.45)	3.15(2.52,3.93)	3.55(2.58,4.88)	0.000	1.26(1.06,1.50)
<i>P</i> for trend	0.000	0.000	0.000		0.000	0.000	0.000		0.000
<i>P</i> -interaction		0.000				0.000			
	WC levels				WC levels				
	Normal	Central obesity			Normal	Central obesity			Normal
No-exposed	1.00(reference)	1.85(1.48,2.31)			1.00(reference)	1.84(1.47,2.30)			1.00(reference)
Fetal exposed	1.21(0.97,1.49)	2.54(1.99,3.24)			1.21(0.98,1.50)	2.53(1.98,3.23)			1.21(0.97,1.49)
Childhood-exposed	1.25(1.06,1.47)	2.92(2.43,3.50)			1.25(1.06,1.47)	2.85(2.38,3.43)			1.25(1.06,1.47)
Adolescence/adult-exposed	1.09(0.92,1.29)	2.93(2.43,3.53)			1.08(0.91,1.29)	2.84(2.34,3.43)			1.09(0.92,1.29)
<i>P</i> for trend	0.000	0.000			0.000	0.000			0.000
<i>P</i> -interaction	0.000				0.000				0.000
BMI: body mass index; WC: waist circle.									
^a Unadjusted; age-adjusted by design									
^b Adjusted for age, educational levels, marital status, place of residence;									
^c Adjusted for age, educational levels, marital status, place of residence, smoking habits, drinking habits, eating meals, social and leisure activities, experience									

Discussion

In our study, we found that the participants exposed to famine in early life had increased risk of dyslipidemia in females, but decreased risk of dyslipidemia in males. After adjustment for observed confounders, including age, educational levels, marital status, place of residence, smoking habits, drinking habits, eating meals, social and leisure activities, the experience of a traumatic event, taking physical activity or exercise, and obesity parameters, the associations still existed both in males and females. Additionally, the study showed that there were increased trends in the associations of BMI/WC with dyslipidemia. After adjustment for observed confounders, including age, educational levels, marital status, place of residence, smoking habits, drinking habits, eating meals, social and leisure activities, the experience of a traumatic event, taking physical activity or exercise, and famine exposure, the associations still existed both in males and females. In general, combined associations of obesity parameters and famine exposure with the prevalence of dyslipidemia were observed in our study. When stratified by sex, males and females differed in most of the risks of dyslipidemia from the opposite sex.

The Chinese famine lasted from the late 1950s to the early 1960s, caused over 30 million excess deaths in most areas[31]. Together with present study, most studies have assessed the associations of famine exposure during early life with risk of dyslipidemia in adults, and no consistent associations were observed. Therefore, this research attempted to examine the association analysis between obesity parameters and dyslipidemia based on a population-based cross-sectional study from CHARLS. Our data support a strongly positive combined effect of famine exposure and obesity parameters on dyslipidemia in middle-aged and elderly Chinese. Both nutrition intervention for exposure to the famine in early life and weight reduction in later life may be required to substantially reduce the risk of dyslipidemia in later life.

As the worst famine, the survivors might be healthier than the frail members were kicked out, a finding that is in line with Darwin's theory of survival of the fittest [32]. In this case, the participants exposed to famine in early life should decrease the risk of dyslipidemia in adults. Sex difference in our study is to be expected. Exposure to famine in adolescence/adults decreased the risk of dyslipidemia in males. However, exposure to famine in early life increased the risk of dyslipidemia in females. When facing the later "rich" environment, the risk of dyslipidemia may be increased. The sex-specific effect might also be associated with the hypothesis that parents in China prefer boys to girls traditionally or survivors' bias.

The outcomes are partly in line with previous studies. X. Xin, W. Wang, H. Xu, *et al* [18] found that exposure to the Chinese famine in early life was associated with an increased risk of dyslipidemia in adulthood. However, another study[17] did not find the association between exposure to famine early in life and the increased risk of dyslipidemia in adults. However, when stratified by sex, a significantly increased risk of dyslipidemia in females in the fetal-exposure group compared to females in the nonexposed group was found, but the significant difference was not present among males. Z. Wang, C. Li, Z. Yang, *et al*

[19]reported that exposure to severe Chinese famine early in life was associated with the higher dyslipidemia risk in females in adult, but not in males in adult. Such discrepancies between those studies may be a result of methodological differences in definitions of famine exposure groups and the different sample selection effect. Additionally, these studies have been criticized for not being adjusted the effect of age. To control the potential age confounding, we categorized the famine exposure into four exposure cohorts [no-exposed stage (born between 1963 and 1974), fetal exposed stage (born between 1959 and 1962), childhood exposed stage (born between 1949 and 1958), adolescence/adult exposed stage (born between 1921 and 1948)] based on the birth year. Our results suggested that early famine exposure was associated with an increased risk of dyslipidemia in females. However, exposure to famine in adolescence/adults decreased the risk of dyslipidemia in males. The sex difference of early life famine exposure and dyslipidemia were common in previous studies[17, 19]. Furthermore, exposure to famine during early life exerted more deleterious effects on women than men. This could be explained by the fact the women may suffer more than men during the famine because of the dominance of a patriarchal mentality in China[33]. The potential mechanisms of the relationship between famine exposure in early life and the increased risk of dyslipidemia in later life were still not fully understood. Exposure to famine in early life may lead to altered lipid profiles in adulthood, and exposure to famine during the fetal period significantly increased the risk. "Fetal Origins hypothesis" was that early adaptations in response to malnutrition resulted in metabolic changes, which were beneficial for short-term survival, but could increase the risk of chronic diseases in adults [34, 35]. Animal model[36] has proved that malnutrition in early life could result in modified cholesterol synthesis and elevated plasma cholesterol concentrations. In addition, epigenetic might play a role in the association between famine exposure in early life and dyslipidemia in adults [37].

In our research, participants who were overweight/obesity, and exposed to famine in early life tended to have a higher risk of dyslipidemia prevalence. The results indicated the good nutrition in adults did not match poor nutrition in early life, which might elevate the relative risk of early life in later life. Furthermore, our data support a strongly positive combined effect of famine exposure and obesity parameters on dyslipidemia in middle-aged and elderly Chinese. However, the previous studies had only focused on the relationship between famine exposure and health outcomes in late adolescence and adulthood. Most of the previous studies meant exactly that: famine exposure was at a higher risk for health outcomes in late adolescence and adulthood. Exposure to Chinese famine in early life was related to increased risk of metabolic syndrome[30, 38–43], weight gain [44–49], diabetes[10, 50–64], hypertension[13, 14, 65–74], cognitive decline[15, 16, 75–79], depressive syndrome[31, 75, 80, 81]. Interestingly, we found that males who were normal weight and exposed to famine in adolescence/adult tended to have a lower risk of dyslipidemia prevalence, and males who were obesity, and no-exposed to famine tended to have the greatest risk of dyslipidemia prevalence. The combined effects differed from the trend of risk in females.

There were several limitations to the study. First, selection bias was to be considered: famine may weed out the frail members of the population and leave the healthier ones. Second, famine exposure for each individual was unknown. Third, not all families were equally affected by famine exposure. However, the results provided large cohort data that could be explored further in the combined effect of famine exposure and obesity parameters on dyslipidemia. Moreover, a significant strength of the study is the large sample of 9427 middle-aged and older Chinese. Another strength is the analytical method the controlled of the potential confounders.

Conclusions

Our data support individual and combined associations of obesity parameters and famine exposure with the prevalence of dyslipidemia in middle-aged and elderly Chinese. Both nutrition intervention for exposure to the famine in early life and weight reduction in later life may be required to substantially reduce the risk of dyslipidemia in later life.

Abbreviations

World Health Organization, WHO; CHARLS, China Health and Retirement Longitudinal Study; BMI, body mass index; waist circle, WC; BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure; M, mean; unstandardized, B; CDC, Centers for Disease Control and Prevention; NSFC, The National Natural Science Foundation of China; National Institute on Aging, NIA; World Bank, WB; Frozen plasma low-density lipoprotein cholesterol, LDL-c; high-density lipoprotein cholesterol, HDL-c; triglycerides, TG; total cholesterol, TC; National Cholesterol Education Programme, NCEP; Adult Treatment Panel III, NCEP ATP III; CVD, cardiovascular disease.

Declarations

Ethics approval and consent to participate

All data are openly published as microdata at <http://opendata.pku.edu.cn/dataverse/CHARLS> with no direct contact with all participants. The Ethics Committee of the China Centre for Economic Research at Peking University approved this study. All the research program for involving humans was in accordance with guidelines of national/international/institutional or Declaration of Helsinki. Written informed consent was obtained from all participants.

Consent to publish

Not applicable.

Availability of data and material

The datasets generated and/or analysed during the current study are available in the CHARLS repository, <http://opendata.pku.edu.cn/dataverse/CHARLS>.

Competing interests

All authors report no potential conflict of interest relevant to the research.

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Authors' contributions

Conceived and designed the research: LZ and H-y L. Wrote the paper: LZ. Analyzed the data: LZ. Revised the paper: LZ, J-l L, L-l G, L Y, C-z W, TY, Dm Z, H-h W, JL, Y-x L, LS, X-p L, YH, H-y C, and Y-z L. All authors reviewed the manuscript.

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