

ORIGINAL RESEARCH ARTICLE

Mediating role of systemic inflammation in heavy metal-induced metabolic dysfunction-associated steatotic liver disease: Insights from NHANES 2017–2020

Supplementary Files

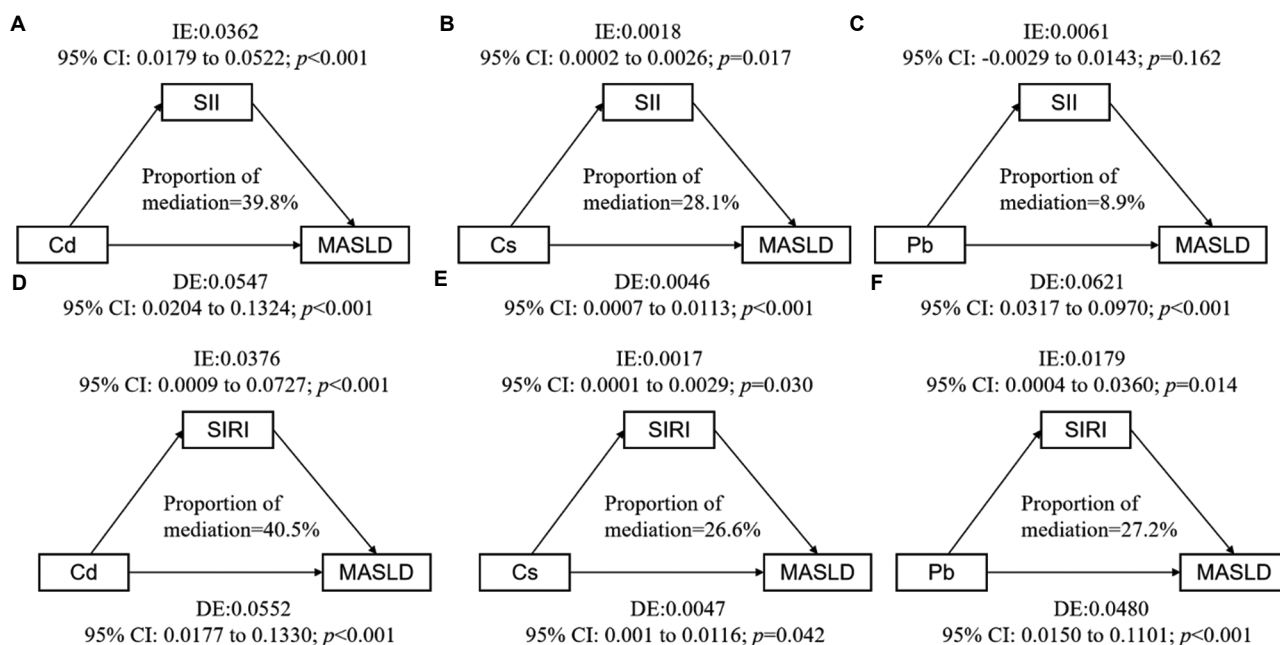


Figure S1. Mediating effect of the relationship between urinary cadmium (Cd), cesium (Cs), and lead (Pb) and MASLD risk. In this figure, the SII indexes were used as intermediaries in (A-C); the SIRI indexes were used as intermediaries in (D-F). The indirect effect (IE) was estimated, and the direct effect (DE) was estimated. The models were adjusted for sex, age (continuous), race, marital status, education, body mass index (continuous), alcohol use, and smoking status.

Abbreviations: MASLD: Metabolic dysfunction-associated steatotic liver disease; SII: Systemic immune-inflammation index; SIRI: Systemic inflammatory response index.

Table S1. Systemic inflammation markers as mediators of the associations between single metals and metabolic dysfunction-associated steatotic liver disease risk

Metals	SII	p-value	SIRI	p-value
	Estimation% (95% CI)		Estimation% (95% CI)	
Ni				
Total effect	-0.0117 (-0.0216 --0.0021)	0.016	-0.0117 (-0.0224--0.0025)	0.012
Indirect effect	0.0003 (-0.0003-0.0011)	0.36	0.0003 (-0.0001-0.0011)	0.188
Direct effect	-0.012 (-0.0219--0.0023)	<0.001	-0.012 (-0.0226--0.0031)	<0.001
Ba				
Total effect	0.006 (-0.0027-0.0152)	0.198	0.006 (-0.0033-0.0151)	0.232
Indirect effect	0.0000 (-0.0006-0.0005)	0.84	-0.0001 (-0.0005-0.0005)	0.882
Direct effect	0.006 (-0.0027-0.0151)	0.194	0.0059 (-0.0032-0.015)	0.222
Co				
Total effect	-0.0057 (-0.0372-0.0074)	0.418	-0.0057 (-0.037-0.0067)	0.44
Indirect effect	0.0011 (0.0001-0.003)	0.01	0.001 (0.0001-0.0026)	<0.001
Direct effect	-0.0068 (-0.0396-0.0064)	0.328	-0.0067 (-0.0387-0.0058)	0.352
Cd				
Total effect	0.0909 (0.0449-0.1377)	<0.001	0.0928 (0.0443-0.1391)	<0.001
Indirect effect	0.0362 (0.0179-0.0522)	<0.001	0.0376 (0.0009-0.0727)	<0.001
Direct effect	0.0547 (0.0204-0.1324)	<0.001	0.0552 (0.0177-0.133)	<0.001
Cs				
Total effect	0.0096 (0.081-0.0125)	<0.001	0.0064 (0.0013-0.0117)	<0.001
Indirect effect	0.0018 (0.0002-0.0026)	<0.001	0.0017 (0.0001-0.0029)	0.03
Direct effect	0.0046 (0.0007-0.0113)	<0.001	0.0047 (0.001-0.0116)	0.042
Hg				
Total effect	0.0025 (-0.0252-0.0331)	0.834	0.0026 (-0.0261-0.0337)	0.888
Indirect effect	-0.0032 (-0.0058--0.0012)	<0.001	-0.003 (-0.0064--0.0008)	<0.001
Direct effect	0.0057 (-0.0214-0.036)	0.648	0.0056 (-0.0231-0.0363)	0.722
As				
Total effect	0.0013 (0.0001 -0.0025)	0.02	0.0013 (0.0001-0.0025)	0.028
Indirect effect	-0.0001 (-0.0004-0.0001)	0.432	0 (-0.0001-0.0001)	0.5
Direct effect	0.0014 (0.0002-0.0026)	0.028	0.0013 (0.0001-0.0025)	0.034
Cr				
Total effect	0.0103 (-0.0093-0.0545)	0.328	0.0103 (-0.0088-0.0576)	0.282
Indirect effect	0.0005 (-0.0003-0.0021)	0.268	0.0008 (0-0.0032)	0.052
Direct effect	0.0098 (-0.0101-0.0539)	0.34	0.0095 (-0.0101-0.0571)	0.328
I				
Total effect	0.0005 (-0.0003-0.0013)	0.264	0.0005 (0.000-0.0013)	0.204
Indirect effect	0.0001 (0.0000-0.0001)	0.078	0.0002 (0.000-0.0006)	<0.001
Direct effect	0.0004 (-0.0003-0.0013)	0.31	0.0003 (0.000-0.0009)	0.27
Mo				
Total effect	-0.0006 (-0.0014-0.0001)	0.096	-0.0004 (-0.0008-0.0001)	0.076
Indirect effect	-0.0002 (-0.0006-0.0001)	0.142	-0.0001 (-0.0003-0.0001)	0.126
Direct effect	-0.0004 (-0.0008-0.0001)	0.11	-0.0003 (-0.0008-0.0001)	0.098

(Cont'd...)

Table S1. (Continued)

Metals	SII	<i>p</i> -value	SIRI	<i>p</i> -value
	Estimation% (95% CI)		Estimation% (95% CI)	
Mn				
Total effect	-0.0006 (-0.0785-0.0787)	0.99	-0.0005 (-0.0807-0.076)	0.98
Indirect effect	0.0008 (-0.0048-0.0073)	0.848	0.0044 (-0.0004-0.0128)	0.076
Direct effect	-0.0013 (-0.0766-0.0774)	0.986	-0.0049 (-0.0819-0.0702)	0.876
Pb				
Total effect	0.068 (0.0315-0.1114)	<0.001	0.0659 (0.0306-0.1124)	<0.001
Indirect effect	0.0061 (-0.0029-0.0143)	0.052	0.0179 (0.0004-0.036)	0.014
Direct effect	0.0621 (0.0317-0.097)	<0.001	0.048 (0.015-0.1101)	<0.001
Sn				
Total effect	0.008 (-0.0045-0.0189)	0.228	0.0073 (-0.0047-0.0185)	0.198
Indirect effect	0.0012 (0.000-0.0029)	<0.001	0.0003 (-0.0002-0.0012)	0.234
Direct effect	0.0066 (-0.0055-0.0183)	0.266	0.0069 (-0.0051-0.0179)	0.224
Sb				
Total effect	0.0166 (-0.2044-0.2255)	0.892	0.0172 (-0.1855-0.2282)	0.82
Indirect effect	-0.0076 (-0.0242-0.0067)	0.284	-0.0031 (-0.0159-0.0106)	0.55
Direct effect	0.0242 (-0.198-0.2336)	0.826	0.0203 (-0.1845-0.2327)	0.792
TI				
Total effect	-0.0156 (-0.1475-0.1074)	0.806	-0.0149 (-0.1377-0.1109)	0.84
Indirect effect	-0.0057 (-0.0153-0.0017)	0.138	-0.0105 (-0.0217--0.0028)	<0.001
Direct effect	-0.0099 (-0.1409-0.1112)	0.866	-0.0044 (-0.1251-0.1223)	0.96
W				
Total effect	-0.0707 (-0.1859-0.0293)	0.192	-0.0707 (-0.183-0.0339)	0.222
Indirect effect	-0.0063 (-0.0143--0.0067)	<0.001	-0.0046 (-0.0111--0.0002)	0.036
Direct effect	-0.0644 (-0.1798-0.036)	0.232	-0.0661 (-0.1777-0.0404)	0.254
Mixed metals				
Total effect	0.097 (0.0349-0.1673)	<0.001	0.0845 (0.0312-0.1421)	<0.001
Indirect effect	0.0561 (0.0155-0.1392)	<0.001	0.0551 (0.0007-0.1279)	<0.001
Direct effect	0.0409 (0.0138-0.0824)	<0.001	0.0294 (0.0062-0.0796)	<0.001

Abbreviations: As: Arsenic; Ba: Barium; Cd: Cadmium; CI: Confidence interval; Co: Cobalt; Cr: Chromium; Cs: Cesium; Hg: Mercury; I: Iodine; Mn: Manganese; Mo: Molybdenum; Ni: Nickel; OR: Odds ratio; Pb: Lead; Sb: Antimony; SII: Systemic immune-inflammation index; SIRI: Systemic inflammatory response index; Sn: Tin; TI: Thallium; W: Tungsten.