

Circulating miR-let-7c is related with proinflammatory state and cardiometabolic risk in adults from a population-based survey in Brazil

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Circulating microRNA (miRNA) are post-transcriptional modulators of gene expression with potential use as risk prediction biomarkers for metabolic alterations⁽¹⁾. Recent evidence shows that members of the let-7 family of miRNA are critically involved in inflammation⁽²⁾, hypertension⁽¹⁾, coronary artery disease⁽¹⁾ and atherosclerosis⁽¹⁾. Consequently, the objective of this study was to investigate the relationship between circulating miR-let-7c, measures of adiposity, lipid profile and inflammatory state in adults. This study analysed 192 individuals, aged 20–59 years, mean body mass index: 26.3 kg/m² (95% CI: 25.44, 27.15) from 2015 ISA-Nutrition survey⁽³⁾, a household cross-sectional, population-based survey of residents from the urban area of São Paulo, Brazil. Participants did not have major systematic disease as acute inflammatory or thyroid diseases; cancer; use of antibiotics, anti-inflammatory, immunomodulators, antiretrovirals; chronic alcoholism; or were pregnant/lactating women. Plasma IL-1 β , IL-6, IL-10, TNF- α , monocyte chemoattractant protein-1 (MCP-1), plasminogen activator inhibitor-1 (PAI-1), intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule 1 (VCAM-1), adiponectin and leptin concentrations were determined by immunoassays.

Plasma C-reactive protein was quantified by enzyme-linked immunosorbent assay. The expression of miR-let-7c-5p in plasma was assessed by RT-qPCR, and Spike-in cel-miR-39 and UniSp6 were used as reference controls for normalisation. Relative miRNA expression was calculated using the 2^{- $\Delta\Delta$ CT} method. The Stata somersd module was used to calculate confidence intervals for Kendall's tau-a to estimate correlations between miR-let-7c and anthropometric, lipid and inflammatory variables (Stata, version 17.0, StataCorp). Most participants had raised waist circumference (67.7%) (\geq 80 cm for women or \geq 90 cm for men), low HDL-c concentrations (51.1%) and high LDL-c concentrations (52.1%), and approximately 30% had increased plasma triacylglycerol concentrations. miR-let-7c expression was positively correlated with both body weight (tau-a: 0.13; 95% CI: 0.02, 0.25) and waist circumference (tau-a: 0.11; 95% CI: 0.00, 0.22) ($P < 0.05$). In addition, miR-let-7c expression correlated positively with triacylglycerol (tau-a: 0.25; 95% IC: 0.15, 0.36; $P < 0.001$), total cholesterol (tau-a: 0.11; 95% IC: 0.00, 0.22; $P < 0.05$) and non-HDL-c (tau-a: 0.16; 95% IC: 0.06, 0.27; $P < 0.01$) concentrations and negatively with HDL-c concentration (tau-a: -0.16; 95% IC: -0.26, -0.06; $P < 0.01$). No significant relationship was found with LDL-c concentration. miR-let-7c expression also correlated positively with PAI-1 (tau-a: 0.17; 95% IC: 0.06, 0.28; $P < 0.01$) and negatively with both adiponectin (tau-a: -0.13; 95% IC: -0.23, -0.04; $P < 0.01$) and VCAM-1 (tau-a: -0.12; 95% IC: -0.22, -0.02; $P < 0.05$). There were no significant correlations between miRNA expression and the other measured inflammatory biomarkers. In conclusion, this study provides evidence that miR-let-7c expression in plasma is related to cardiometabolic risk through relationships with a proinflammatory state, abnormal blood lipid concentrations, excess body weight and abdominal adiposity.

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