## Low high-density lipoprotein cholesterol, but not high low-density lipoprotein cholesterol, associates with systemic metabolic alterations

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**Aim:** Dyslipidemia encompasses various forms of lipid abnormalities and represents a central component of metabolic syndrome. The relationship between dyslipidemia subtypes and broader metabolic profiles is poorly characterized in modern populations. This study provides a comprehensive metabolic characterization of patients presenting with distinct dyslipidemic patterns – low high-density lipoprotein cholesterol (HDL-c) and elevated low-density lipoprotein cholesterol (LDL-c) – at a dedicated tertiary-center outpatient clinic.
**Methods:** Patients evaluated at the Metabolic Health Clinic of San Raffaele Hospital, Milan, between January 2023 and October 2024, were included. Medical history, anthropometrics (i.e. body mass index, BMI, and waist circumference), serum lipids and liver enzymes were recorded. Patients with low HDL-c or high LDL-c, as defined according to current guidelines, were compared to patients with normal values. Network analysis identified patient distinct metabolic clusters.
**Results:** A total of 496 individuals were included. Patients with low HDL-c levels (n=193, 38.9%) exhibited higher BMI (28.6 vs 25.6 kg/m$^2$, p<0.001), waist circumference (100.0 vs 94.0 cm, p<0.001), ALT levels (28.0 vs. 23.0 U/L, p<0.001), and triglycerides (146.0 vs. 99.0 mg/dL, p<0.001), and a greater prevalence of fatty liver disease (33% vs. 21%, p 0.006) and arterial hypertension (51% vs. 39%, p 0.012) than those with normal HDL-c levels. HDL-c showed significant inverse correlations with both BMI (R coefficient -0.272, p<0.0001) and waist circumference (R coefficient -0.325, p<0.0001). Network analysis highlighted strong associations among HDL-c, triglycerides, ALT levels, BMI, and waist circumference. Conversely, high LDL-c levels, found in 382 (77%) patients, showed no association with metabolic parameters.
**Conclusions:** Low HDL-c was associated with obesity, central adiposity, hypertriglyceridemia, and fatty liver disease. In striking contrast, LDL-c appears to be independent of these metabolic alterations. These findings underscore the interconnectedness of HDL-c with the metabolic landscape, while emphasizing the importance of assessing LDL-c levels regardless of patient anthropometrics and metabolic phenotype.

## Single nucleotide polymorphisms (SNPs) in patients with acute ischemic stroke: A prospective study of the relationship between genetic, acute phase cytokine levels and stroke prognosis

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The genetic basis of complex diseases like ischemic stroke probably consists of several predisposing risk factors, such as genes involved in inflammation and thrombotic pathways. Some genetic polymorphisms have been associated with the risk of stroke.
**Aim:** On this basis the aim of this study was to evaluate:
- the frequency of some single nucleotide polymorphisms (SNPs) of genes of pro-inflammatory cytokines and coagulation factors in stroke patients;
- the relationship between each identified SNP and TOAST stroke subtype;
- the relationship between the serum levels of the cytokines analyzed and the diagnostic subtype of ischemic stroke;
- the relationship between the serum levels of the analyzed cytokines and stroke prognosis regarding event recurrence, AMI recurrence, and mortality.

**Materials and methods:** All patients aged > 18 years admitted for acute ischemic stroke in the period between 2011 and 2021 were prospectively enrolled. Each patient was subjected to genetic analysis to evaluate various genetic polymorphisms and to the analysis of the levels of cytokines circulating in the different collection times (T0, T1, and T2). Three different biallelic polymorphisms, of the IL-10 gene were identified.
**Results:** 624 subjects were enrolled, including 429 patients with ischemic stroke and 195 controls. Stroke subtype: 47% LAAS, 27% LAC, and 26% CEI. Regarding the immunoinflammatory variables, patients with CEI showed significantly higher levels of serum glucose and all the cytokines analyzed, compared to patients with both LAC and LAAS.
Logistic regression analysis revealed that elevated IL-10, TNF-alpha, IL-6, and IL-1beta values are predictive of LAAS and CEI subtypes, respectively. IL-10 levels were lower in patients who developed stroke during follow-up, whereas TNF-alpha, IL-1, and IL-6 levels were significantly higher in patients with recurrent stroke at follow-up, who developed a new vascular event or who experienced death during follow-up. From the analysis of the distribution of the genotypic frequencies of the polymorphisms analyzed, a statistically significant difference emerged between the cases and the controls for all the polymorphisms in the genes of pro-inflammatory cytokines, TPA and PAI-1.
These results demonstrated an association between some pro-inflammatory and prothrombotic polymorphisms and the risk of ischemic stroke.