Several studies showed that high-density lipoprotein cholesterol (HDL-C) has anti-inflammatory effect. The neutrophil-lymphocyte ratio (NLR) is a new biomarker of systemic inflammation. The aim of this study was to assess the NLR in healthy participants with low HDL-C. We studied 69 patients with low HDL-C (≤35 mg/dL) and 59 control participants (HDL-C >35 mg/dL) with similar cardiovascular risk factors. Hematological indices were measured in all patients with low HDL-C and control participants. The HDL-C was significantly lower among the patients with low HDL-C than that of the control group (31.7 ± 2.7 vs 50.7 ± 5.0 mg/dL, respectively; P < .001). The NLR was significantly higher among the patients with low HDL-C than that of the control group (2.6 ± 0.8 vs 1.6 ± 0.4, respectively; P < .001). The NLR was negatively correlated with HDL-C (P < .001, r = -.53). The NLR is significantly elevated in patients with low HDL-C when compared with control participants.