
Abstract
We evaluated serum homocysteine concentrations and the C677T polymorphism of the gene encoding for methylene tetrahydrofolate reductase, a key enzyme for homocysteine metabolism, in 57 patients with Cushing’s syndrome, 41 with active disease, and 16 in remission after successful surgery and 105 blood donors. The patients with active Cushing’s syndrome had significantly higher serum homocysteine levels and lower folate concentrations than either the patients in remission or controls. The presence of a statistically significant difference in homocysteine concentrations among the three groups was confirmed after adjustment for confounding variables. In a multiple regression model, homocysteine levels were significantly associated with midnight serum cortisol levels (beta _ 0.33, P _ 0.01), which is the most sensitive marker of endogenous hypercortisolism, and serum folate levels (beta _ 0.32, P _ 0.02). The distribution of methylene tetrahydrofolate reductase genotypes was not different between patients and controls. In conclusion, active hypercortisolism is associated with hyperhomocysteinemia and reduced serum folate concentrations, whereas the patients in remission have homocysteine concentrations comparable with healthy subjects. Low serum folate concentrations do not fully account for the increase in homocysteine levels that are positively correlated with cortisol levels. Hyperhomocysteinemia may be key to the prothrombotic state and increased cardiovascular risk of Cushing’s syndrome.