In diabetes, the levels of advanced glycation end products (AGEs) increase as a result of chronic hyperglycemia (1). The best-characterized receptor for AGEs is RAGE. The AGE-RAGE interaction mediates activation and secretion of various cytokines via activation of factors such as the nuclear factor-kB, leading to a proinflammatory process (1). A guanine-to-adenine single nucleotide polymorphism at codon 82 (GGC→AGC) located in exon 3 of RAGE causes the amino acid change glycine to serine (Gly82Ser or G82S polymorphism) within the putative ligand-binding domain of the protein (2). The RAGE Ser82 isoform has been suggested to upregulate the inflammatory response upon engagement of S100/calgranulins, thereby contributing to the enhancement of proinflammatory mechanisms (3). The aim of this study was to investigate the association of the RAGE polymorphism Gly82Ser with type 1 and type 2 diabetes in a Brazilian population compared with a nondiabetic sample.

**RESULTS** — Nonproliferative diabetic retinopathy was found in 15.4% of the diabetic patients and proliferative retinopathy in 12.4%. Furthermore, 0.9% of the diabetic patients had macrovascular disease, 19.6% had microalbuminuria, and 18.2% had either macroalbuminuria or overt renal insufficiency. We found two genotypes in the population studied: homozygotes for the Gly82 isoform of RAGE (GG) and heterozygotes Gly82/Ser82 (GS). There were no differences in the genotype frequencies (96.3% GG, 3.7% GS) among the Euro Brazilians and one (type 2 diabetic) among Asians. The Gly82Ser polymorphism was not found in the African-Brazilian population. Further investigation of the frequency of this polymorphism in African Brazilians must be conducted to clarify the significance of this finding. The genotype frequency of the Gly82Ser polymorphism in this Brazilian population is similar (P > 0.05) to that found in Asian nondiabetic subjects (10%) (2), Caucasian-English type 2 diabetic subjects (7%) (2), Asian-Indian nondiabetic subjects (2%) and type 2 diabetic subjects with retinopathy (7%) (5), Finnish nondiabetic subjects (7%) (6), Caucasian-Czech nondiabetic subjects (0.7%) (4), American-Caucasian nondiabetic subjects (6.9%) and type 2 diabetic subjects (7.9%) (7), and Caucasian-Danish type 1 diabetic subjects with nephropathy (5.9%) (8). However, the frequencies found in this study were significantly lower (P < 0.05) when compared with Chinese nondiabetic (40.4%) and type 2 diabetic (32.3%) subjects (9), Japanese nondiabetic (34.6%) and type 2 diabetic (21.6%) subjects (10), Finnish subjects with coronary heart disease with or without type 2 diabetes (12 and 15%, respectively) (6), Asian-Indian type 2 diabetic subjects without retinopathy (18%) (5), the nondiabetic Caucasian-English population (12%) (2), and Caucasian-Danish type 1 diabetic subjects without nephropathy (9.4%) (8). We found no association of the GS genotype with diabetes complications. However, the lack of clear associ-
ation of the RAGE polymorphism with diabetes complications may be due to the low frequencies observed in all groups studied.

**CONCLUSIONS** — In conclusion, our data indicate that the Gly82Ser polymorphism of the RAGE gene is not associated with either type 1 or type 2 diabetes in a Brazilian sample, suggesting that this single nucleotide polymorphism may not be associated with development of the disease in this population. Furthermore, our results suggest a very low frequency of the Gly82Ser polymorphism in the African-Brazilian population. This is the first frequency study of the Gly82Ser RAGE polymorphism in a Brazilian population.

**References**


