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OBJECTIVES

Diabetic nephropathy is the leading cause for end-stage renal disease requiring renal replacement therapy. Currently identified risk factors do not fully explain the susceptibility of some patients to diabetic nephropathy. Peroxisome proliferator-activated receptor g (PPARg) Pro12Ala gene polymorphisms modulate insulin sensitivity and oxidative stress in diabetic patients.

Several polymorphisms in another immune modulatory set of genes, the C–C chemokine receptor 5 (CCR5) genes, were associated with diabetic nephropathy. However, CCR5δ 32 gene polymorphisms were not studied in patients with diabetic nephropathy.

The aim of this study was to assess the association between polymorphisms in both PPARg Pro12Ala and CCR5δ 32 genes and the presence of diabetic nephropathy in Egyptian patients with type 2 diabetes.

METHODS

We included 51 patients diagnosed with type 2 diabetes of at least 5 years duration. They were all normotensive patients with no other clinically identifiiable risk factor for kidney disease from the outpatient clinic. Genotype detection for PPARγ Pro12Ala and CCR5δ32 gene polymorphisms were carried out by PCR. Clinical data, HbA1c, lipid profile, fasting and postprandial blood sugar were recorded. Serum creatinine and urinary albumin/ creatinine ratio were measured to stratify the participants according to the presence or absence of diabetic nephropathy.

RESULTS

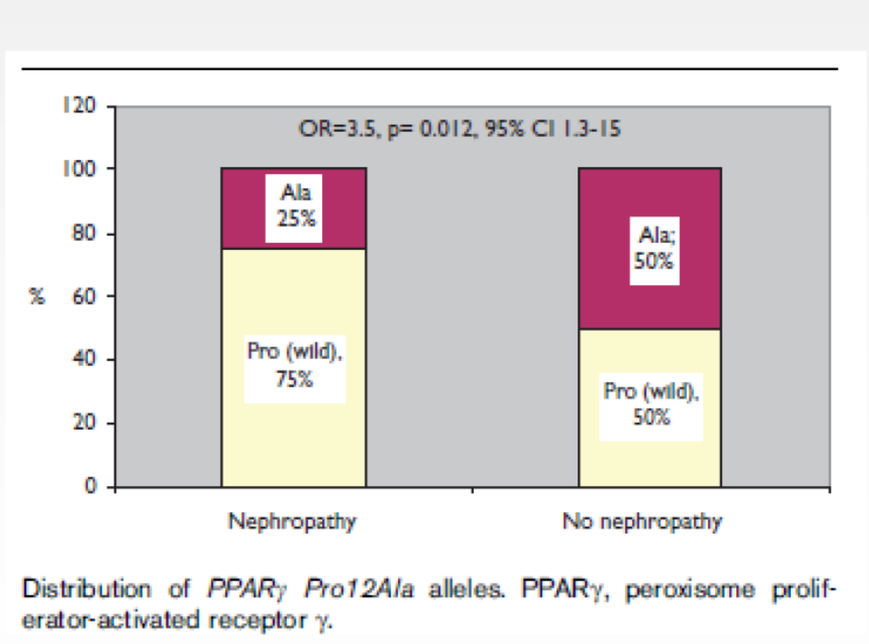
Age, sex, BMI, HbA1c, and duration of diabetes were not significantly different among patients with and those without diabetic nephropathy. Diabetic nephropathy patients had a significantly higher urinary albumin/creatinine ratio and lower estimated glomerular filtration rate levels (Po0.0001).

Homozygotes for the PPARg Pro12Ala Pro–Pro allele constituted 82% of our total study population and 86.4% of patients with diabetic nephropathy; the remaining were Pro–Ala heterozygotes, and we had no Ala–Ala homozygotes. The odds ratio for diabetic nephropathy in Pro–Pro homozygotes was 3.5 (P= 0.075, 95% confidence interval, 0.8–15). The Pro allele was present in 75% of patients with nephropathy and 50% of those without nephropathy. The Pro allele was significantly associated with diabetic nephropathy compared with the Ala allele (odds ratio = 3.5, P = 0.012, 95% confidence interval, 1.3–15).

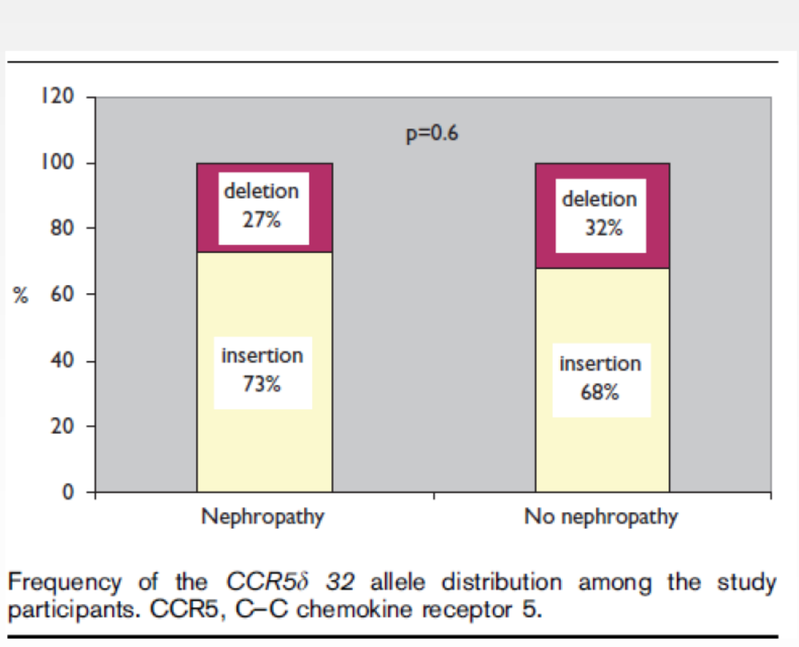
Regarding the CCR5 δ 32 insertion/deletion genotype, 24 patients were homozygous for the insertion polymorphism, two were homozygous for the deletion polymorphism, and the remaining 25 were insertion/deletion heterozygotes. There was no significant difference between nephropathic and non-nephropathic patients as regards the CCR5d 32 genotype (P= 0.3) or the frequency of allele distribution (P= 0.6).

CONCLUSIONS

The Pro allele of PPARg Pro12Ala was associated with diabetic nephropathy. Polymorphisms in the CCR5d 32 gene did not show an association with diabetic nephropathy.



Distribution of *PPARγ Pro12Ala* alleles. PPARγ, peroxisome proliferator-activated receptor γ.



Frequency of the *CCR5δ 32* allele distribution among the study participants. CCR5, C–C chemokine receptor 5.

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