STUDY OF β2-ADRENERGIC RECEPTOR POLYMORPHISMS AMONG HYPERTENSIVES

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INTRODUCTION

- Polymorphisms within Beta2-adrenergic receptor (β2AR) gene have been repeatedly linked to hypertension *(Ranade et al., 2001, Kazuk et al., 2005).*
- Among the β2AR polymorphisms detected, Arg16Gly and Gln27Glu codons were considered the two most important variations. Arg16Gly especially, has been found to be significantly associated with hypertension in Caucasian and African subjects *(Hong xie. et al., 1999, Gerfried et al., 1999).*
- The amino acid substitution at these codons may lead to abnormal regulation of β2AR activity *(Garovic et al., 2002).*
- The estimated frequencies of variant alleles Gly16 and Glu27 in Malaysian subject were 47% and 6.8% respectively *(Nik Nor Izah., 2009).*

OBJECTIVE

- The aim of the present study was to assess the association between β_2AR polymorphisms and hypertension in our population.

METHODS

- 100 subjects were included in this study. Hypertensive patient samples were recruited from governmental clinics in Kuantan-Pahang.
- 5ml of blood was taken from patients. The sample was subjected to DNA extraction by using Magtration system .
- Quantity and quality of DNA was measured by using biophotometer plus device.
- Genotyping was done using polymerase chain reaction (PCR) based on restriction fragment length polymorphism (RFLP) assay.
- The two SNPs at codon 16 & 27 was genotyped by amplifying 107 and 353 base pair by hot start Master Mix in 20µl reaction volume .

RESULTS

There were no significant evidence of association in allelic and genotypes distribution of Arg16Gly and Glu27Gln with elevated blood pressure and hypertension (Table 1).

Table 1.

SNPs	Genotype	MAF	Allele OR (%95 CI)	p value
Gly16Arg	GG/GA/AA			
Case	14/23/13	0.490	0.817 (0.468-1.426)	0.78
Control	17/22/11	0.440		
Gln27Glu	CC/CG/GG			
Case	1/5/44	0.070	1.811 (0.682-4.811)	0.37
control	1/10/39	0.120		

To validate the PCR-RFLP genotype at codons 16 and 27, four randomly chosen samples were subjected to automated direct nucleotide sequencing. The results show concordance findings with PCR-RFLP

Figure 1.

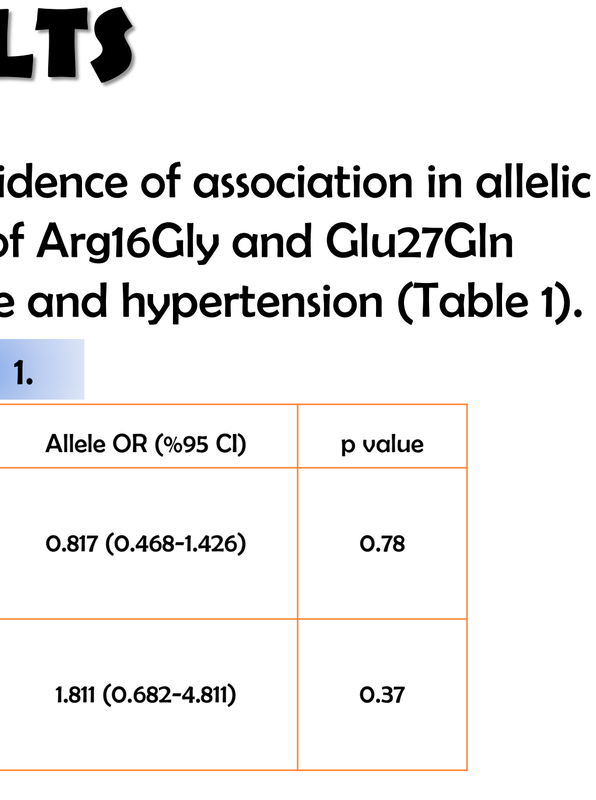

Figure 1

PCR-RFLP assay result for selected markers in β2AR gene. A: codon16 PCR product. B: lane 1, Arg16Arg; lane 2, Gly16Gly; lane 3, Arg16/Gly16. C: codon27 PCR product. D: lane 1, Glu27Glu; lane 2, Gln2Gln; lane 3, Glu27Gln27.

Figure 2.

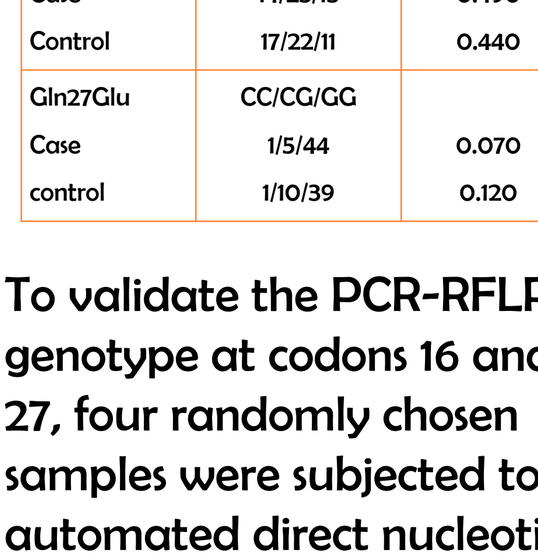

Figure 2

Direct nucleotide sequencing of selected sample. A: Homozygous wild type (Arg16). B: Homozygous TAG to TGG transition resulting change of Arginine to Glycine at codon 16 (Gly16). C: Homozygous Glu27. D: Heterozygous TTG to TTC transition resulting in possible Glutamine to Glutamic acid at codon 27 (Gln27Glu).

CONCLUSION

- These findings suggest that the variation within codon 16 and 17 of β2AR gene were unlikely to confer genetic susceptibility for hypertension in our population samples.
- The negative association in our study was corresponded to that reported in other Asian populations *(Jia et al., 2000., Norihiro et al., 2001).*

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