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Brief Report

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Impact of Apurinic/Apyrimidinic Endonuclease *Asp148Glu (rs3136820)* Gene Polymorphism and APE1 Level in Depression Disorders Patients

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Abstract

The repair system processes are very important in the maintenance of genome against mutagenic factors, the present study deal with Apurinic/apyrimidinic endonuclease gene polymorphism and its level in depression disorder patients, blood samples were collected from patients and control to serum separation for APE1 detection and DNA extraction for APE1 *Asp148Glu (rs3136820)* gene polymorphism by CTTP-PCR technique, finding of present research show that the mean age of patients and control were non-significant differences (P 0.156), the BMI was significant differences (P 0.042) between groups. non- significant decrement was appeared in the APE1 level in the patients group (P 0.183), the CTTP-PCR products show two alleles (T and G) and three genotyping in addition to deletion mutation (TT, GT and GG), significant differences was observed in TG allele that low frequent in patients than the control group (OR 5.0909, CI% 1.3190-19.649, P 0.0182). The GG allele shows high frequent in patients than the control group in non-significant differences (OR 3.8500, CI 95% 0.7614-19.468, P 0.103). Deletion mutation also found in non-significant differences (OR 1.7143 CI% 0.1305-22.5139, P 0.6816). The effect of APE1 genotyping in APE1 level show non-significant differences in APE1 levels, according to APE1 genotyping (P 0.870) although of decreasing the level of APE1 in TG in patients than other genotyping. There was a weak relation of APE1 levels, and no association between APE1 *Asp148Glu (rs3136820)* genotyping with depression disorder.

Keywords: Apurinic/apyrimidinic endonuclease • *Asp148Glu (rs3136820)* • Gene polymorphism • APE1 level • Depression disorders patients • CTTP-PCR

Introduction

The Apurinic/apyrimidinic endonuclease gene encodes the major AP endonuclease in human. It's used in DNA repair in DNA damage lesions by the Base Excision Repair (BER) pathway in cell nucleus and mitochondria [1], the AP Endonuclease 1 (APE1) is enzyme having more than one functions, it's a member of the BER pathway, in addition to DNA repair activity, it has a role in the reductive many transcription factors activations [2], there are regions encoded the tow function of APE1 the redox function encoded by N-terminal region and the repair function encoded by C-terminal [3,4].

The psychiatric diseases have been found to associate with accumulated DNA damage and impaired in DNA rapier, these damages are caused by oxidative stress and the brain neurons found to be more vulnerable to oxidative destruction than other cells, resulted to pronounced neuropathology, like mutations, dysfunction in some cells and aberrant phenotypes [5-10].

Depression disorders have been recorded in high incidence in Iraq after COVID-19 era which leads to lifestyle alteration in population, thus the present study was suggested to evaluate the Apurinic/apyrimidinic endonuclease gene polymorphism in APE1 level in depression disorder patients.

Materials and Methods

Sample collection and study sitting: the present study, including 20 cases (male) have age range (20 years to 66 years) years and 25 healthy contributors have age range (19 years to 58 years), patients suffered from depression disorder symptoms who attended to the privet Psychiatric Clinic and diagnosis by A specialist doctor, blood samples were collected according to ethical approval of the ministry of environment and health of Iraq, blood samples divided into two parts, for sera isolation and DNA extraction, both parts stored -20°C until its used.

APE1 level detection

The APE1 detected by ELIZA by E6642Hu kit provided from bioassay technology Lab with high sensitivity (0.099 ng/ml).

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DNA extraction

About 200 µl of blood was used to DNA extraction with proteinase K according to manufacture leaflet (favorgen), the concentration and purity were detected using Nano drop.

Oligos and PCR experiment

The APE1 *Asp148Glu (rs3136820)* polymorphism using the following primers that provided from macrogene company 5′-CCT ACG GCA TAG GTG AGA CC; R1:5′-TCC TGA TCA TGC TCC TCC-3′; F2: 5′-TCT GTT TCA TTT CTA TAG GCG AT; R2: 5′-GTC AAT TTC TTC ATG TGC CA [11]. The final concentration of Oligos aliquot was 10 p/µl, the CTTP-PCR was used annealing Tm 58ºC to amplification target loci, the products were Three bands a 236 bp, 167 bp and a 360 bp band for T allele, G allele and common band respectively.

Gel electrophoresis

Agaros was used to visualize the extraction DNA and the amplification products using 70 V, 20 mA, 1% agaros, 0.5X TBE buffer for 45 min and ethidum bromide staining.

Results

The results of present research show that the mean age of patients and control were (39.500 ± 3.104), (33.88 ± 2.436) in non-significant differences (P 0.156), the BMI was (25.01 ± 0.864) for patients and (27.41 ± 0.759) for control in significant differences (P 0.042). Also non- significant decrement was appeared in APE1 level in patients group (P 0.183) (Figure 1).

The DNA extracted from whole blood show concentration ranged (65 ng/µl to 130 ng/µl) and purity ranged (1.6-2.3), on band was observed for each sample (Figure 2A). The PCR products show two alleles (T and G) and three genotyping in addition to deletion mutation (TT, GT and GG) (Figure 2B).

The statistical analysis of genotyping in patients and control groups is clarified in Table 1, significant differences was observed in TG allele that low frequent in patients (20%) than control (56%) (OR 5.0909, CI% 1.3190-19.649, P 0.0182). The GG allele shows high frequent in patients (35%) than control (15%) in non-significant differences (OR 3.8500, CI 95% 0.7614-19.468, P 0.103). Deletion mutation also found in (20%) and (4%) in control group in non-significant differences (OR 1.7143 CI% 0.1305-22.5139, P 0.6816), the allele frequency show that G more frequent in patients than T allels (Table 1).

The effect of APE1 genotyping in APE1 level was detected for study subjects, there was non-significant differences in APE1 level according to APE1 genotyping (P 0.870) although of decreasing the level of APE1 in TG in patients than other genotyping (Figure 3).

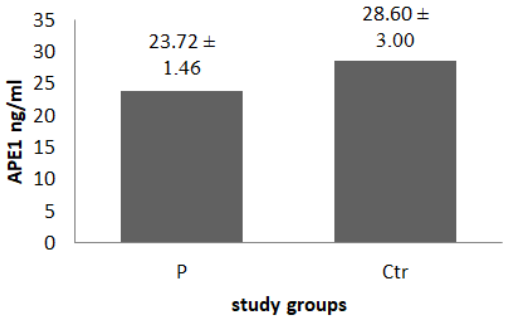
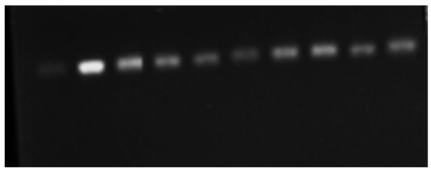
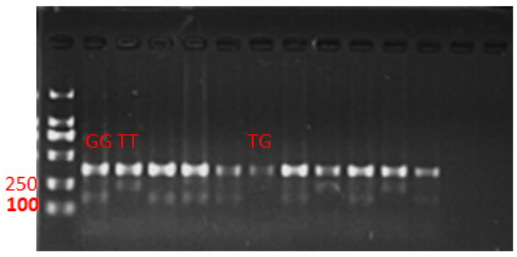


Figure 1. The APE1 level in study groups (mean ± SE, independent t test, p<0.05).



A

Figure 2A. Gel electrophoresis of DNA extracted from whole blood for study groups.



B

Figure 2B. Gel electrophoresis of CTTP-PCR products of APE1 gene polymorphism for study groups (70 V, 20 mA, 1% agaros, 0.5X TBE buffer for 45 min).

Table 1. The APE1 *Asp148Glu (rs3136820)* gene polymorphism in study groups.

Genotyping	Patients (%)	Control (%)	Odd ratio (CI%)	Sig
TG	4(20%)	14(56%)	5.0909 (1.3190-19.649)	0.0182
TT	5(25%)	7(28%)		
GG	7(35%)	3(15%)	3.8500 (0.7614-19.468)	0.1030
G	0.562	0.416		
T	0.437	0.583		
Deletion mutation	4(20%)	1(4%)	1.7143 (0.1305 to 22.5139)	0.6816

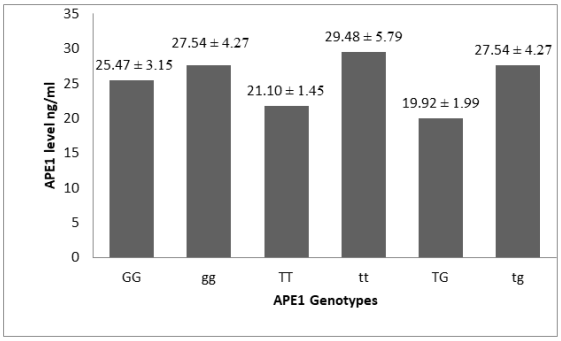


Figure 3. Effect of APE1 *Asp148Glu (rs3136820)* genotypes in APE1 levels in study groups (GG, TT and TG) in patients (gg, tt and tg) in control group (mean ± SE, ANOVA one way, at p<0.05).

Discussion

The present suggestion was conducted to estimate the an important repair enzyme with its encoded gene in subjects with depression regarding to prolonged psychological stress lead to increased oxidative stress which may be caused DNA mutation, present finding shows non-significant decreased in APE1 level in patients, the depletion of APE1 was found to be associated with neuronal death after ischemic brain injury [12]. Stetler, et al. indicated that the DNA repair enzymes like APE1 stimulation was a unique strategy for neuroprotection against hippocampal injury [13]. Take together APE1 is a critical cellular protein has multifunction like a transcriptional cofactor, and a suppressor of ROS by a redox site [14], these functions could lead to neuro-protection independent of DNA repair. Investigations clarified that the deficiency in the expression and activity of APE1 exacerbates oxidative injury in multiple models, including neurons [15-17]. The depletion in APE1 may be contributed in depression due to its role in the neuron cells protection against high level of oxidative stress biomarkers that have been proved in patients group (data not shown). The APE1 *Asp148Glu (rs3136820)* genotyping show non-significant association with depression patients in present finding, another study show a significant association between repair genes and schizophrenia included APE1 [18]. The polymorphism in DNA repair genes may be effected in protein levels which contributed in rapier pathway have been associated with different disease like neurological disorders [19] like Alzheimer's disease [20], Parkinson's disease [21] and Huntington's disease [22], the impact of *(rs3136820)* in the APE1 level show that tg, tt and d genotyping have a higher level than others and (TT and TG) genotyping were low frequent in patients than the control group, thus the lower level of APE1 in patients may be because more frequent of these genotyping in the patients group. Other DNA repair enzyme genes also studied in Iraqi Depression patients; the results show no association between RAD-18 and XRCC1 genotyping [23]. The relation between APE1 gene polymorphism with depression didn't observe in the previous studies [24,25].

Conclusion

The association of DNA repair with some disease should be validated; the present study needs more investigations to prove other APE1 SNPs relation relations to depression disorder especially suffered from unbalanced in oxidative stress. However, it can be concluded that the APE1 level and APE1 *Asp148Glu (rs3136820)* genotyping may have an effect in the depression disorders and contributed in its pathology.

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