Faculty of Science
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Association between Corin and Cardiovascular Disease in Type-2 Diabetic Palestinian Patients

Thesis

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I declare that this thesis has been composed and the work recorded here has been done by myself. It has not been submitted for any other degree at this or any other university.

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Abstract

Cardiovascular diseases (CVD) are the highest-incidence cause of death and morbidity in patients with type 2 diabetic (T2DM). The natriuretic peptide is important in controlling blood pressure and salt water balance. Both corin and furin are involved in cleave pro-atrial natriuretic peptide (ANP) and pro-BNP (Brian natriuretic peptide) into their active forms (ANP and BNP). The human corin gene is on chromosome 4p12-13, which has 22 exons and spans approximately 200 kb in length. Single-nucleotide polymorphisms in the corin gene were found to alter corin protein structure and impair its biological activity. It has been suggested that corin defects could contribute to CVD.

Methods: This study included 75 subjects divided into three groups; 25 healthy subjects as controls (Gr I); 25 T2DM patients without no medical history of CVD (Gr II) and 25 T2DM patients confirmed diagnosis of CVD (Gr III). All groups were matched for age and gender. All subjects were investigated for biochemical markers, serum corin, furin and BNP levels were determined By ELISA techniques. Two corin gene SNPs (1757C>T and 1796A>C) were genotyped

using allele specific oligonucleotide-polymerase chain reaction (ASO-PCR).

Result: Glycated haemoglobin, fasting plasma glucose, serum creatinine, serum total cholesterol and LDL-C levels were significantly increased while HDL-C level was significantly decreased in all T2DM patients compared to the control group. Also, serum uric acid and triacylglycerols showed significant only in T2DM patients with cardiovascular complications compared to the control group.

Human corin level in T2DM patients with and without CVDs was significantly lower than the control group, while furin and BNP levels were significantly higher in T2DM with CVDs compared to T2DM patients without CVDs and control groups. There was significant negative correlation between serum corin and BNP levels in T2DM patients with and without CVDs while there was a significant positive correlation between serum furin and BNP levels in T2DM patients with and without CVDs and control groups. Both furin and BNP were found to be more sensitive than corin (80% vs. 56%, $p<0.01$), whereas furin showed high specificity when compared to BNP (96% vs. 84%, $p<0.05$) and corin (96% vs. 64%, $p<0.0001$) in predicting

cardiovascular complications in T2DM patients. Corin gene SNPs are not associated with serum corin levels.

Conclusions: Results of this study suggested that serum furin and BNP associated with CVD development but furin showed high specificity so, it may be serve as a biomarker in CVDs diagnoses in T2DM patients.

Key words: Corin, Furin, Cardiovascular disease, Type-2 Diabetic, Palestinian

List of Abbreviations

Abbrev.	Full-term
ACC	American College of Cardiology
ACEI	angiotensin-converting enzyme inhibitor
ACR	Albumin/creatinine ratio
ACTH	adrenocorticotropic hormone
ADA	American diabetes association
ADH	Antidiuretic hormone
ADHF	Acute decompensated heart failure
ADP	Adenosine diphosphate
AHA	American Heart Association
AMP	Adenosine monophosphate
ANOVA	One-way analysis of variance
ANP	Atrial natriuretic peptides
ARB	Angiotensin-receptor blocker
ASO-PCR	Allele specific oligonucleotide-polymerase chain reaction
AST	Aspartate transaminase
ATP	Adenosine triphosphate