

Relation between Blood Pressure Control and Insulin Secretion Markers among Elderly Diabetic Females

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Abstract

Background: Hypertension is a common condition among elderly individuals, often present concurrently with diabetes or a part of metabolic syndrome, and each can accelerate the progression of the other. The importance of identifying the relation between blood pressure control and insulin secretion abilities is of utmost importance to decrease progression of vascular complications among diabetics.

Aim: To identify the prevalence of hypertension and detect the relation between blood pressure control and insulin secretion markers including C-peptide (CP) levels and C-peptide index (CPI) among elderly diabetic females

Methods: A cross sectional study conducted from the first of October, 2014 to the end of March, 2016, where 163 elderly diabetic females were recruited from the Inpatient wards of Ain shams university hospital at that time. They underwent careful history taking, blood pressure measurement and assessment of insulin secretion including fasting serum C-peptide and CPI measurement in addition to assessment of glycemic control by fasting blood sugar (FBS) estimation.

Results: 82.8 % of our participants were hypertensives, 32.5% had uncontrolled systolic blood pressure and 33.7% had uncontrolled diastolic blood pressure, there was statistically significant difference between uncontrolled and controlled systolic and diastolic blood pressure as regard insulin secretion indicators including fasting serum CP level and CPI.

Conclusions: Hypertension is a common health problem among diabetic female geriatric population, and its presence and even control could be related to insulin secretion markers such as fasting serum C-peptide level and CPI value.

Keywords: C-peptide index. insulin secretion in hypertensive elderly

Background

Ageing is a universal phenomenon; almost 5.3% of the entire population is a major concern to health economists¹. By 2020 it will be 177 million elderly people, aged above 60 years. Ageing process is as such complex and multi-factorial. Chronic morbidities like diabetes and hypertension are becoming common health problems among the geriatric population².

High geriatric population means a higher number of patients with various chronic diseases and increasing percentage of lifetime health care costs are accounted for this population. Longevity will have a greater chance of developing diseases that occur more commonly during later life; many individuals will also live with chronic illnesses³. Of all the diseases, diabetes mellitus is one of the most common diseases affecting a large number of

elderly populations along with hypertension which play a major role on the quality of life of the elderly and the healthcare costs. Centers for Disease Control and Prevention (CDC) suggest that the prevalence of diabetes will double in the next 20 years, in part due to the aging of the population⁴.

Several studies showed a significant association between residual beta-cell function and various vascular complications of diabetes including hypertension that is confirmed in a large clinical cohort study of patients with type 1 diabetes,¹⁰. In contrast to these studies in type 1 diabetes, several studies¹¹⁻¹³ have reported conflicting results on the association between serum C-peptide levels and vascular complications in type 2 diabetes.

C-peptide concentrations in the peripheral blood are widely accepted as the most appropriate measure of insulin secretion because it is secreted in equimolar amounts with insulin and is not removed in the first pass through the liver^{5,6}. Moreover, evidence indicates that C-peptide is not merely an inactive by-product of insulin biosynthesis but also a hormonally active peptide itself⁷⁻⁹. C peptide index (CPI) could be used as an index of endogenous insulin secretion, it is not affected by exogenous insulin therapy, hence its value in patients with insulin therapy¹⁴.

The aim of this study was to identify the prevalence of hypertension and to evaluate the relationship between glycemic control and insulin secretion abilities and control of hypertension among Egyptian elderly diabetic female patients.

Method:

This study is a descriptive cross-sectional study. One hundred and sixty three elderly diabetic females were recruited from the first of October 2014 to the end of March, 2016 from Inpatient wards of Ain Shams University Hospital.

After obtaining an informed consent, all participants underwent careful history taking including history of DM and hypertension. All included patients were diabetics on antidiabetic treatment and the associated hypertension was evaluated based on history of hypertension, being on antihypertensive medications and on blood pressure measurement with a calibrated sphygmomanometer at resting state, hypertension was defined as a systolic pressure above or equal 140 mmHg and/or a diastolic pressure above or equal 90 mmHg¹⁵. Accordingly, participants were divided into 2 groups hypertensive and normotensives, and based on the current blood pressure, hypertensive patients further divided into 4 groups: the first 2 groups included patients with controlled and uncontrolled systolic blood pressure, and the second 2 groups included patients with controlled and uncontrolled diastolic blood pressure. Then comparison was done between each of the 2 groups of patients as regards fasting blood sugar and insulin secretion indicators.

All patients underwent assessment of glycemic control by fasting blood sugar estimation utilizing enzyme technique with gluco- oxidasis. We used fasting serum C-peptide and CPI as indicators for insulin secretion, accordingly fasting serum C-peptide and CPI measurement were done for each participant. Blood samples were withdrawn during fasting state after about 8 hours fasting, then collected into plain tubes and centrifuged to separate serum that is stored at -70°C until analysis then referred to Ain shams university hospital blood lab for determination of fasting serum C-peptide level using C-peptide kits manufactured by DRG instruments GmbH, Marburg, Germany and were analyzed by ELISA methods. The C-peptide index (CPI)

was calculated for all participants with the following formula: fasting C-peptide (ng/ml)/fasting glycemia (mg/dl) × 100^{16,17}.

Statistical method

Values were presented as means + SD or as numbers and proportions, as appropriate. The relations between qualitative variables were evaluated by Chi-square test or Fisher's exact test, as indicated. Means were compared with Student's test or analysis of variance. Quantitative variables were correlated with the use of coefficient of correlation "r". All tests were bilateral and a P value of 0.05 was the limit of statistical significance. Analysis was performed by statistical package software IBM-SPSS for MAC, version 24.

Results:

The study was conducted on 163 elderly diabetic females with a mean age of 66.14 (±5.71). Mean systolic blood pressure 128.67±19.35, mean diastolic blood pressure 79.51±11.00. Mean serum fasting blood sugar was 174.62 (±84.67), serum C peptide (ng/mL) was 2.78 (±3.63), CPI was 1.85 (±2.65) (Table 1).

Table (1): Clinical characteristics of the patients according to studied variables:

Variables	Descriptive Statistics			
	Range	Mean	±	SD
Age	60 - 85	66.19	±	5.72
Systolic blood pressure	80 - 210	128.56	±	19.35
Diastolic blood pressure	50 - 100	79.39	±	11.08
Fasting blood sugar	43 - 460	174.20	±	84.58
C peptide (ng/mL)	0.00 - 19.55	2.77	±	3.62
CPI	0.00 - 19.79	1.84	±	2.64

Out of the 163 subjects, 135 patients (82.8%) were hypertensives and based on their current blood pressure control, patients were divided into four groups: controlled systolic blood pressure 50.3% (n= 82) and uncontrolled systolic blood pressure 32.5 % (n= 53), and patients with controlled diastolic blood pressure 49.1 % (n= 80) and uncontrolled diastolic blood pressure 33.7% (n= 55) (Table 2).

Table (2): Classification of hypertensive cases based on blood pressure control.

Controlled systolic blood pressure N (%)	50.3% (n= 82)
Uncontrolled systolic blood pressure N (%)	32.5 % (n= 53)
Controlled diastolic blood pressure N (%)	49.1 % (n= 80)
Uncontrolled diastolic blood pressure N (%)	33.7% (n= 55)

There was statistically significant inverse correlation between C peptide and patients' age ($r=-0.16$, p value 0.03) (Figure 1) and statistically significant positive correlation between C peptide and CPI ($r=0.88$, p value 0.000) (Figure 2).

Figure (1): Correlation between age and C peptide.

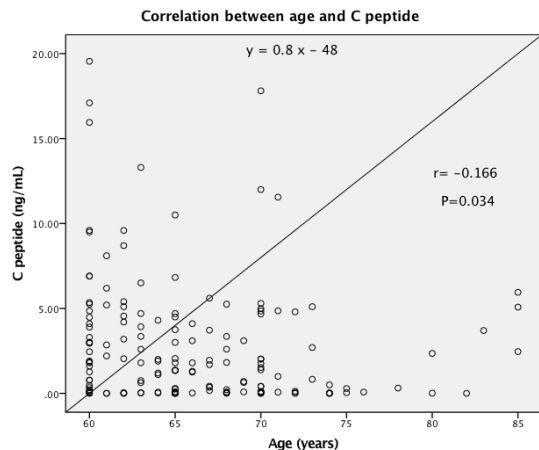
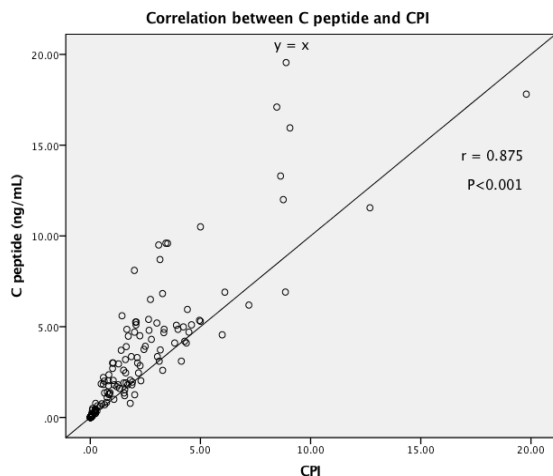


Figure (2): Correlation between C peptide and CPI.



Upon comparison between hypertensive cases ($n=135$, 82.8%) and normotensive cases ($n=28$, 17.2%), there was no statistically significant difference between the 2 groups as regards FBS, C peptide (ng/mL) and CPI. Means of FBS were 172.12 ± 79.70 versus 184.21 ± 106.17 ($p= 0.49$). The mean serum levels of C peptide ng/ml and CPI were $(2.80 \pm 3.57$ and 1.88 ± 2.70) versus $(2.62 \pm 3.95$ and $1.64 \pm 2.35)$ ($p= 0.81$ and 0.65), respectively (Table 3).

Based on blood pressure control, there was statistically significant difference between controlled and uncontrolled diastolic blood pressure as regard means of serum C peptide level and CPI ($p<0.001$). The mean serum levels of C peptide ng/ml and CPI were $(3.33 \pm 3.91$ and 2.25 ± 3.13) versus $(2.02 \pm 2.86$ and $1.35 \pm 1.84)$, respectively. Patients with controlled diastolic blood pressure had significantly higher C peptide

($P=0.036$) and CPI values ($P=0.037$), compared to uncontrolled patients (Table 4).

Table 3: Comparison between hypertensives and normotensives

variables	Hypertensive (n=135)	Normotensive (n=28)	P value
	Mean \pm SD	Mean \pm SD	
FBS	172.1 \pm 79.70	184.2 \pm 106.1	0.49
C peptide (ng/mL)	2.80 \pm 3.57	2.62 \pm 3.95	0.81
CPI	1.88 \pm 2.70	1.64 \pm 2.35	0.65

Table (4): Comparison between uncontrolled and controlled diastolic blood pressure

Based on diastolic blood pressure				
variables	Uncontrolled (n=55)	Controlled (n=80)	P value	
	Mean \pm SD	Mean \pm SD		
FBS	164.2 \pm 70.53	177.5 \pm 85.45	0.34	
C peptide (ng/mL)	2.02 \pm 2.86	3.33 \pm 3.91	0.03	
CPI	1.35 \pm 1.84	2.25 \pm 3.13	0.03	

Upon comparison between means of serum C peptide level and CPI in both groups of systolic blood pressure, there was statistically significant difference between controlled and uncontrolled systolic blood pressure ($p<0.001$). The mean serum levels of C peptide (ng/ml) and CPI were $(3.44 \pm 4.07$ and 1.80 ± 2.31) vs $(2.02 \pm 3.19$ and $1.13 \pm 1.44)$, respectively (Table 5).

Table (5): Comparison between uncontrolled and controlled systolic blood pressure

Based on systolic blood pressure				
variables	Uncontrolled (n=53)	controlled (n=82)	P value	
	Mean \pm SD	Mean \pm SD		
FBS	175.4 \pm 84.20	169.9 \pm 77.10	0.70	
C peptide (ng/mL)	1.80 \pm 2.31	3.44 \pm 4.07	0.004	
CPI	1.13 \pm 1.44	2.37 \pm 3.19	0.003	

Discussion

Hypertension is a common comorbidity among persons with diabetes and its prevalence increases with advancing age. In diabetic people, hypertension is a major risk factor for cardiovascular disease. Elderly patients with hypertension and DM have an increased mortality risk than similarly aged controls without DM. The United Kingdom Prospective Diabetes Study blood-pressure trial demonstrated the benefits of more intensive blood pressure control in individuals with type 2 diabetes. Hence, detection of hypertension amongst the diabetics and maintaining its control is essential for reducing mortality of these patients^{18,19}

In this study, the concentrations of fasting serum C peptide level and CPI value were used as surrogate markers of beta-cell function, as serum C-peptide level is

commonly considered an index of insulin secretion, it is higher in the elderly persons than young population²⁰ that is consistent with our finding of the statistically significant positive correlation between serum C peptide and age.

We have 82.8% elderly diabetic female patients who are hypertensive, and about 66.3% had uncontrolled blood pressure which is consistent with Jain and Paranjape, 2013 who found that 80% of studied diabetic elderly population were hypertensive⁴.

This study examined difference between hypertensive and normotensive elderly diabetic female patients in fasting serum blood sugar, C peptide level and CPI value, in addition to the association between poor blood pressure control and poor glycemic status and / or lower insulin secretion markers.

Both serum C peptide and CPI could be used as surrogate markers for endogenous insulin secretion and pancreatic beta cells function¹⁴ that is supported by our finding of the statistically significant positive correlation between serum C peptide and CPI.

We could not demonstrate significant association between control of blood pressure and glycemic status assessed by FBS. While other studies showed significant association between glycemic control and blood pressure in elderly diabetic patients such as Yoda et al.²⁴ who examined association between glycemic control and morning blood pressure in 50 elderly diabetic patients and showed significant association between morning blood pressure surge and poor glycemic control including higher fasting blood sugar and HbA1c.

This study did not show significant difference between hypertensive and normotensive elderly diabetic female patients as regards glycemic control and insulin secretion markers, but showed significant differences between elderly patients with uncontrolled and controlled systolic and diastolic blood pressure in fasting serum C peptide level and CPI value this agreed with a population based study that found that elderly diabetic female patients with controlled systolic and diastolic blood pressure had significantly higher fasting serum c peptide level and CPI value indicating better pancreatic beta cells function and higher insulin secretory abilities, supporting the beneficial effects of C-peptide in attenuating the pro-atherogenic risk in diabetes by inhibiting insulin-induced neo-intima formation⁹.

Although some previous studies showed that increases in serum C-peptide are related to increases blood pressure^{11,13}. In a recent cross sectional study, 471 type 1 diabetic patients were followed from 1994 to 2004, subjects with the lowest fasting C-peptide levels were found to have the highest rate of micro vascular complications¹⁰.

In a large community-based survey of adults in china, was conducted by the Yang-Ming Crusade in 1992 and 1994 among a total of 1,447 men and 1,800 women

(mean age 46.7 years), found that fasting C-peptide was significantly higher among hypertensive subjects in comparison to normotensives (p= 0.00)²².

Similarly, Gonzalez-Mejia et al.²³ found that C-peptide was significantly higher in insulin resistance syndrome subjects (P<0.05) and C-peptide correlated with all components of insulin resistance syndrome including hypertension.

Further prospective studies are needed to confirm the association of C-peptide and hypertension, other micro and macro vascular complications in patients with diabetes and to elucidate the causal relationship between C-peptide and blood pressure in diabetes mellitus.

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