Research Article

Vascular Endothelial Growth Factor as Predictive Marker for Hypertension in Iraqi Adults Patients

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Abstract

Background: Vascular endothelial growth factor (VEGF) is considered the most potent angiogenic growth factor for the stimulation of collateral vessel growth in peripheral and myocardial ischemia and other coronary heart disease.
Aim: The aim of the present study was first to assess the levels of VEGF in adult subjects with hypertension, second to find any correlation between VEGF and other studied biochemical markers.
Patients & Methods: Thirty four adults with hypertension (age mean 34.55 ± 3.79 year) from outpatients of Al-yarmook Teaching Hospitals in Baghdad were selected randomly from March to April 2015. For comparison, (30) normotensive subjects which were matching to patients in age and BMI. VEGF levels were measured.
Results: Biochemical parameters include FBG, HDL, and cholesterol, TG, HbA1c and PCV. Anthropometric measurements were also recorded. VEGF significantly higher ($p < 0.05$) in patients group when compared to healthy group, as well as, significant elevation also shown in FPS, HDL and HbA1c, while TG, cholesterol, Creatinine and PCV not affected.
Conclusion: VEGF can be used as diagnostic marker for the hypertension in adult patients.

Key words: Hypertension, VEGF

INTRODUCTION

Idiopathic hypertension is the type of hypertension that by definition has no identifiable cause. It is the most common form of hypertension [(1)], it have a tendency to be familial (90-95%) and is likely to be result of an interaction between environmental and hereditary factors [(2)]. Prevalence of hypertension increased with age [(3)], and subjects with high blood pressure at younger ages are at risk for the rapid development of the events that follow hypertension [(4)]. Hypertension can increase the risk of kidney, cerebral and cardiac disorders [(5)]. In people aged 18 years or older, hypertension can be defined as a systolic and/or a diastolic blood pressure measurement firm higher than an accepted normal range (currently 139 mmHg systolic, 89 mmHg diastolic. Lower edge are used (135 mmHg systolic or 85 mmHg diastolic) if measurements are taken from 24-hour either home monitoring or ambulatory [(6)].

In the last decade, many young Iraqis individuals are suffering from hypertension for unknown reasons and through done all examinations to find the cause which leading to rise blood pressure, as these cases needed to find a vital function to help early detection of high blood pressure. Data indicate increased vascular resistance in hypertension refers to vascular mechanisms as possible potential reasons for high blood pressure [(7)].

Vascular endothelial growth factor (VEGF), basically known as vascular permeability factor (VPF) [(8)], is a transit peptide produced by cell types which induces vasculogenesis and angiogenesis. It is part of the system that retrieves the oxygen supply to tissues when blood circulation is insufficient. Cellular biological functions of VEGF including activation of the mitogen-activated protein kinase, protein kinase C which leads to cell survival, proliferation, the generation of nitric oxide and prostacyclin and angiogenesis [(9)]. Serum VEGF level is markedly increase in diabetes mellitus [(10)] and asthma

[(11)]. VEGF's function is to generate new blood vessels during embryonic development, after injury and collateral circulation [(12)]. VEGF tends to have a protective role on cardiac microcirculation, but its action mechanisms on cardiac function and morphology in cardiovascular disease patients are not clear [(14)].

The current study sought to test the hypothesis that circulating VEGF levels could influence the cardiac performance in hypertensive patients.

PATIENTS AND METHODS

The patients were recruited from out-patient clinic of Al-Yarmouk Teaching Hospital in the period from April to June 2015. Thirty four Iraqi hypertensive adult subjects were entered in the study as well as 30 healthy person for comparison. All patients were newly diagnosed and not take any drugs (any drugs effects on our data). The diagnosis of hypertension was formerly done by physicians. About (5 ml) venous blood was drown from each patients and healthy subjects.

PCV test was down directly, VEGF was done by using enzyme linked immune sorbent assay ELISA, (Ray biotech Co., USA). Biochemical testing included plasma fasting blood glucose , fasting serum lipid (triglycerides), HDL, total cholesterol and serum creatinine were done by spectrophotometer technique (Spinreact Co., Moroco). Glycated HbA1c % was done by using a diagnostic Human Kit Laboratories (Germany).

Statistical analysis

Statistical analysis was performed using SPSS-21 (Statistical Packages for Social Sciences- version 21). Unpaired t-test was used to assess significant difference between means. $P < 0.05$ was considered statistically significant. Receiver operation characteristic method (ROC curve) was performed by MedCalc -12 program (IBM corp 2012).

RESULT

The characteristics of hypertensive patients and healthy subjects summarized in table (1). Patients and control group were similar in regard to age and BMI with no significant difference [P value >0.05].

The serum VEGF levels were markedly elevated in the patients group when compare to healthy subjects group (mean ± SD: 241.5 ± 87.24 pg/ml versus 188.8 ± 43.71 pg/ml respectively, [$p < 0.01$], Figure 1).

Table (1): Distribution of different parameters in patients and control groups.

	Group	N	Mean	Std. Deviation	Std. Error Mean	P value
Age (years)	Control	30	34.8	3.57	0.65	0.79
	Patient	34	34.5	3.79	0.65	
BMI	Control	30	27.5	0.91	0.16	0.08
	Patient	34	28.0	1.13	0.19	
Heart Rate	Control	30	79	4.93	0.90	0.02*
	Patient	34	82	4.75	0.81	
FBG (mg/dl)	Control	30	81	9.76	1.78	0.002*
	Patient	34	89	9.78	1.67	
(TG) (mg/dl)	Control	30	133.8	22.02	4.02	0.25
	Patient	34	139.8	19.61	3.36	
Cholesterol (mg/dl)	Control	30	176.6	12.11	2.21	0.14
	Patient	34	180.7	10.35	1.77	
HDL (mg/dl)	Control	30	54.83	10.63	1.94	0.008*
	Patient	34	48.58	7.42	1.27	
Cr (mg/dl)	Control	30	0.85	0.11	0.02	0.46
	Patient	34	0.83	0.12	0.02	
VEGF (pg/ml)	Control	30	188.8	43.71	7.98	0.004*
	Patient	34	241.5	87.24	14.96	
HbA1c%	Control	30	5.1	0.34	0.06	0.006*
	Patient	34	5.4	0.26	0.04	
PCV	Control	30	47.6	1.15	0.21	0.88
	Patient	34	47.5	1.32	0.22	

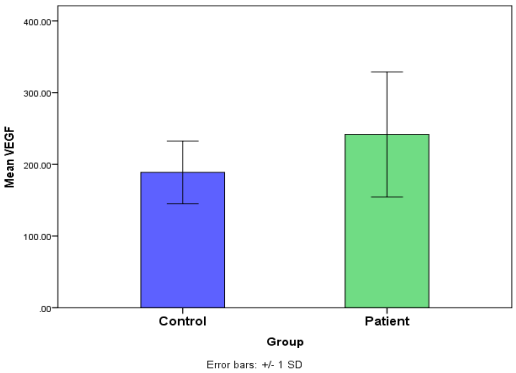

Figure (1): Values for VEGF in patients and control group

Receiver Operator Curve (ROC) Analysis also done to find the sensitivity and specificity of VEGF in hypertensive patients (52.9 and 86.7, respectively), as shown in figure (2), table (2).

. **Table (2): Area under the ROC curve (AUC)**

Area under the ROC curve (AUC)	0.718
Standard Error	0.0649
95% Confidence interval	0.591 to 0.823
z statistic	3.352
Significance level P (Area=0.5)	0.0008

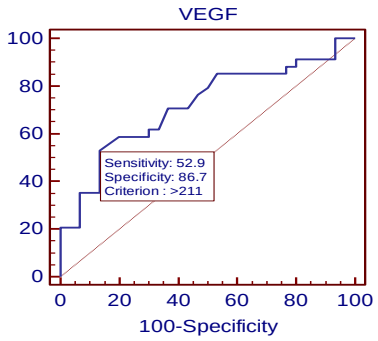

Figure (2): Receiver Operator Curve for VEGF

Table (1) also shown that there was a significant difference in the HDL levels between patients and control groups [p value < 0.01], as well as , serum FBG and HbA1c also significantly elevated in patients group when compared to healthy subjects group [p value < 0.01]. Unlike the means of TG, cholesterol, Cr. and PCV levels did not show a significant variation between patients and controls.

There was no significant correlation between VEGF [pg/ml] with TG [r=0.280, p=0.109], cholesterol [r=0.142, p=0.422], HDL [r=-0.149, p=0.399], S.Creatinine [r=-0.039, p=0.828] , HbA1c [r=0.189,p=0.286] and PCV [r=0.216, p=0.219] in patients while there was a significant positive correlation between VEGF and FBG [r=0.422, p< 0.05] in patients and there was no correlation in control group as shown in table (2).

Table (2): The correlations between VEGF and other studied parameters in patients.

Variable	VEGF *[pg / ml]* Pearson Correlation	*Sig. (2-tailed)*
FBG	0.422*	0.013
TG	0. 280	0.109
Cholesterol	0.142	0.422
HDL	-0.149	0.399
S.Cr	-0.039	0.828
HbA1c	0.189	0.286
PCV	0.216	0.219

DISCUSSION

The main finding of the present study was that the patients with high blood pressure had markedly increased VEGF serum levels when compared with the control subjects. Vascular endothelial growth factor acting via VEGFR2, plays a critical role in influencing basal levels of blood pressure control by enhancing NO synthase expression and NO activity [(14)]. Kucukardali Y *et al* (2008) recorded that VEGF rise in patients with established cardiovascular disease may be used as an indicator of the need for revascularization[(15)]. VEGF is considered the most potent angiogenic growth factor for the stimulation of collateral vessel growth in peripheral and myocardial ischemia. However, there is accumulating evidence that VEGF is strongly expressed in atherosclerotic vessels and can enhance neoangiogenesis in atherosclerotic plaque [(16)]. Recent study suggested that VEGF stimulates nitric oxide production [(17)]. Fulton D reported that increased free VEGF levels in preeclampsia might lead to suppressed NO signaling, causing systemic rise blood pressure [(18)].

Glycolated hemoglobin significantly elevated in hypertensive patients in comparison to control groups, although the values within the normal range. The current study reported that there was a significant decrease in the mean of HDL in patients group when compared to control this finding is agree with other study which suggested that dyslipidemia was reported as a risk factor for incident hypertension in a few prospective studies, that lead to increase in triglycerides and decrease in high-density lipoprotein cholesterol (HDL-C) so the triglycerides to HDL-C ratio (TGs)/HDL-C can be used as predictors of hypertension among Middle Eastern people [(19)]. High-density Lipoproteins, HDL, kind of cholesterol "cleans" the cholesterol that is in the arteries and transfer it to the liver. The decreasing of HDL lead to many events that ending to cardiovascular [(20)]. In accordance with the present data, Several studies that

have noticed that there is a significant decrease in the HDL levels in hypertensive patients when compared to control [21, 22] . For several years the decreasing in of HDL level was associated with an increased risk of expand CVD, principally coronary heart disease [22].

Conclusions: There are significant increase in VEGF levels in patients when compared to control group.

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