Obat: Jurnal Riset Ilmu Farmasi dan Kesehatan
Volume. 3 Nomor. 1 Tahun 2025
e-ISSN : 3031-0148, dan p-ISSN : 3031-013X, Hal. 149-156
DOI: https://doi.org/10.61132/obat.v3i1.984
Available online at: https://journal.arikesi.or.id/index.php/OBAT

Dehydroepiandrosterone Sulfate Deficiencies as Independent Predictors of Increased Coronary Artery Disease in Men with Type II Diabetes Mellitus

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Abstract. *The adrenal cortex synthesis the steroid hormone dehydroepiandrosterone (DHEA), has a significant effect on diabetes mellitus. Our study targeted to estimate the relationship between serum levels of DHEA sulphate (DHEAS) and the risk of CAD complication for T2DM in men. Ninety Iraqi male subjects were divided into three groups. Each group has thirty people: thirty people type 2 with diabetes mellitus, thirty person type 2 diabetes mellitus patients with CAD complications, and the control group has thirty healthy people. A significant decrease ($p<0.01$) of DHEAS, was observed in T2DM with CAD (120.8 µg/dl) compared to both T2DM (141.26 µg/dl) and the control group (239.86 µg/dl). Meanwhile, an increased coronary risk index in T2DM with CAD (10.68) compared to both T2DM (7.56) and control group (4.41) was observed. These findings were confirmed by the negative correlation of DHEAs with coronary risk index. We suggested that a decreased level of DHEAS value may be a beneficial sign for future CAD in patients with T2DM.*

Keywords *: Diabetes, Dehydroepiandrosterone Sulfate, Insulin, Lipid, Complication.*

1. INTRODUCTION

Diabetes has been widely known as an emerging epidemic with a growing effect on nearly every country, age group, and the economy worldwide. Recently, it has been shown that more than 415 million persons worldwide are currently alive with diabetes. [1] Based on the recently reported studies, about half of diabetes patients are not aware of their disease which leads to diabetic complications.[2] Cardiovascular disease is the major cause of mortality and disability among diabetics.

It has been established that the number of cardiovascular diseases (CVDs) will rise with an increase of the number of patients with diabetes. [3, 4] Type 2 diabetes (T2DM) is a metabolic disorder in tissue (muscle, fat, and liver) which characterized by an impaired ability to insulin resistance and secrete insulin.[5] The adrenal cortex produces the steroid hormone dehydroepiandrosterone (DHEA), it has beneficial effects on mellitus diabetes. It has been stated that DHEA-sulfate (DHEA-S) and DHEA increase insulin secretion in the pancreas and insulin sensitivity of the muscle, liver and adipose tissue. [6]

Received: Desember 07, 2024; Revised: Desember 21, 2024; Accepted: Januari 06, 2025; Published: Januari 08, 2025

DHEA exists mostly in its sulfated ester form (DHEAS), the predominant circulation adrenal steroid hormone in healthy individuals. Peak serum concentrations of DHEAS and DHEA began about 25 years of age in both sexes, and from the third century forward, these levels dropped gradually.[7] Despite the massive reported studies about insulin action and DHEA, there are limited studies to support the role of DHEA in the risk of type 2 diabetes remains insufficient, and most of the reports regularly concentrate on women.[8] Numerous studies have shown conflicting results on influence of dehydroepiandrosterone (DHEA) in glucose metabolism. [9, 10, 11]

DHEA-S biochemically enhances lipid profiles in animal models of experimentally induced atherosclerosis. [12] Numerous research have assessed the correlation between DHEA-S levels and coronary artery disease.[13] The Coronary risk index (CRI) (TC/HDL-C) provides a significant indicator to predict the risk of coronary risk diseases. [14] This study focuses on the evaluate the relationship between the risk of CAD complication for T2DM in men and the serum levels of DHEA sulphate (DHEAS).

2. METHODS

The current study included 90 Iraqi male subjects separated into three groups: Thirty type 2 diabetes mellitus patients ages ranged (35-58 years), (30) type 2 diabetes mellitus patients with CAD complications with ages ranging (38-58 years) and the other thirty healthy people are non-diabetic, non-hypertensive, and free from ischemic heart disease, aged between 30 and 57 years. People who have Type 1 diabetes, gestational diabetes, chronic diabetic complications (retinopathy, nephropathy, and neuropathy), malignancies, and type 2 diabetes requiring insulin injections were excluded. Fasting venous blood samples were drawn from all individuals. Serum DHEAs and insulin were performed on the LIAISON analyzer by using chemiluminescent immunoassay (CLIA), Blood sugar profile and lipid profile including fasting blood sugar, HbA1c, cholesterol, triglyceride, HD, LDL, and VLDL were done by COBAS C 111, (Fully Automated). The Coronary risk index was estimated (triglyceride/HDL).

Statistical analysis

The statistical software (SPSS v 19; Chicago, IL, USA) has been used to compare two diabetic patient groups and control (without complication, and CAD complication) in study parameters. The (Analysis of variation- ANOVA) was applied to compare between

means (P value of 0.05) and was considered statistically important. The pearson correlation coefficients of studied parameters were considered important when P< 0.05.

3. RESULTS

This study showed no significant age differences between men in the three groups (p>0.05). Meanwhile, ANOVA analysis showed extremely important differences (p<0.01) in DHEAs, FBS, HbA1c, insulin, and lipid profile cholesterol, triglyceride, HDL. LDL, and VLDL) (Table 1) between three groups.

Table 1: Selected characteristic of study participants

Variable	Group	Mean	± SD	P value
Age (year)	Control	43.03	6.70	0.75
	DM	45.13	6.94	
	DM with CAD	47.03	6.48	
FBS (mg/dl)	Control	87.63	5.505	0.00
	DM	178.93	71.85	
	DM with CAD	211.73	69.95	
HbA1C (%)	Control	5.02	.5917	0.00
	DM	7.65	1.24	
	DM with CAD	8.44	1.146	
Insulin µIU/ml	Control	17.88	5.78	0.00
	DM	1.68	.550	
	DM with CAD	.945	.511	
Cholesterol (mg/dl)	Control	186.76	25.47	0.00
	DM	207.9	60.85	
	DM with CAD	269.06	73.82	
Triglyceride (mg/dl)	Control	174.9	37.43	0.00
	DM	213.8	73.35	
	DM with CAD	285.36	76.58	
HDL (mg/dl)	Control	41.3	6.26	0.00
	DM	30.53	5.43	
	DM with CAD	29.10	5.91	
LDL (mg/dl)	Control	186.76	25.47	0.00
	DM	207.90	60.85	
	DM with CAD	269.06	73.82	
VLDL (mg/dl)	Control	34.98	7.48	0.00
	DM	42.76	14.67	
	DM with CAD	57.07	15.31	
CRI	Control	4.41	1.62	0.00
	DM	7.56	3.86	
	DM with CAD	10.68	4.79	
DEHAs (µg/dl)	Control	239.86	86.64	0.00
	DM	141.26	67.48	
	DM with CAD	120.80	40.64	

The level of DHEAs ranged (95-362) µg/dl with a mean value of 236.86 µg/dl for the control group. A decrease of this value was observed in both patient groups type 2 diabetes mellitus with CAD and type 2 diabetes mellitus (61-278) µg/dl with mean value 141 µg/dl) & (73-219) µg/dl with mean value 120.8 µg/dl) respectively, as shown in Figure 1.

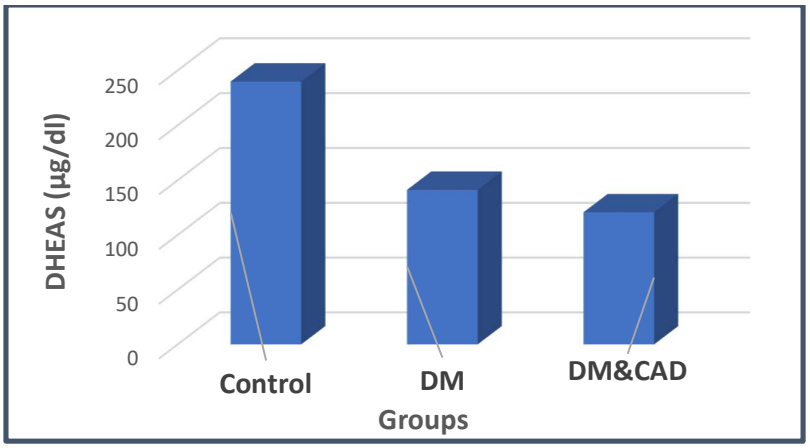

Figure 1: Mean levels of dehydroepiandrosterone sulfate in type 2 diabetes mellitus with CAD, type 2 diabetes mellitus, and control groups.

Table 2: Correlation coefficient of dehydroepiandrosterone sulfate with FBS, HbA1c, insulin, and lipid profile (cholesterol, triglyceride, HDL.LDL, and VLDL)

Variable	Correlation	p value
FBS	-0.439**	0.00
HbA1C	-0.563**	0.00
Insulin	0.603**	0.00
Cholesterol	-0.356**	0.001
Triglyceride	-0.392**	0.00
HDL	.505**	0.00
LDL	-0.356**	0.001
VLDL	-0.392**	0.00
CRI	-0.429**	0.00

**P < 0.01.

The results presented in Table 2 show the correlation coefficient of dehydroepiandrosterone sulfate with FBS, HbA1c, insulin, lipid profile (cholesterol, triglyceride, HDL.LDL, and VLDL) ,and coronary risk index. Where it has been observed highly significant positive correlation of DHEAs with insulin and HDL. While highly significant negative correlation were observed of DHEAs with each of FBS, HbA1c, cholesterol, triglyceride, LDL, VLDL, and CR|I.

4. DISCUSSION

The first thing should be explained is that DHEA and DHEAS considered precursors of sex hormones, also it is not strange that these hormones have to be an important variance between males and females.

In that all studies found that the concentration of these steroids is much increased in males than in female ,and all studies find that the associations between DHEA(S) and health or survival vary by gender [15][15] .Therefore, only men were included in our study to avoid sex differences. The decreased concentration of insulin in diabetic patients in comparison to the control group indicated that in fact the pancreas is unable to produce enough insulin to be insulin resistant. Significant negative correlation of DHEAS with both fasting blood glucose and glycated hemoglobin indicated an important protective role of DHEA hormone to against type 2 diabetes ,and this that finding was agreement with previous much studies for the positive effects of the DHEA in patients with type 2 diabetes.[16] In previous study of Tenenbaum et al. clarify mechanisms of DHEA action that is a peroxisome proliferator-activated receptor (PPAR), reduced the incidence and delayed the onset of type 2 diabetes in patients with impaired fasting glucose levels. [17] Our results showed significant negative correlation of DHEAS with TC, TG, and LDL; and significant positive correlation with HDL This finding agreement with mechanism suggested by Leighton B et al that DHEA prevents accumulation and/or storage of energy as body fat by increasing resting metabolic rate.[18] Indirect effect of this hormone on the peroxisomal β-oxidation pathway in animal experiment was reported.[19] Increases serum levels of the TC, TG, and LDL; and decrease in HDL are major factors for the development of CVDs.[20,21] For type 2 diabetes mellitus (T2DM) patients, raised triglycerides (TG) to high density lipoprotein cholesterol (HDL -C) ratio is a danger influence for coronary artery disease (CAD).[22] This in our line result where, it has been observed significant increase of triglyceride/HDL ratio (CRI) in Type 2DM with CAD compared to both T2DM and control groups. Meanwhile, significant decrease of DHEAS was observed in T2DM with

CAD compared to both T2DM and control groups .These finding confirm by significant negative correlation of DHEAS with CRI which reflect possibility useful DHEAS as a predictor marker of CAD in diabetic patients.

5. CONCLUSION

In our primary study, data suggested that decreased level of DHEAS value might be a beneficial predictor for upcoming CAD in patients with T2DM with. Additional research are needed to support our results.

Acknowledgements

Special thanks to the healthy volunteers and patients who agreed to contribute in the present research.

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