

Role of Stress Situation at Diabetic Nephropathy Development

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Abstract

Background: Diabetic Nephropathy (DN) is disorder occur in renal nephrons caused by diabetes mellitus (DM) disease . Therefore un-control DM consider as high risk factor for developed renal disease , the un-control DM detection by high glycated hemoglobin (HbA1c) level for long periods . Cystatin C is monomeric and non-glycosylated protein many roles in human body such as diagnosis role in renal, heart and neurology diseases . Cortisol is the most important stress hormone ,it's release from adrenal cortex layer to all cells by blood .The functions of cortisol in cells include: regulation of blood sugar levels, metabolic process , anti-inflammatory, and other functions.

Objective of the Study: Explain effect of stress situation on Diabetic Nephropathy disease

Materials and Methods: The present study included 40 DM cases group classified into 20 control DM (without DN) and 20 un-control DM (with DN) ,all subjects age in current study was more than 50 years of both genders. The current study focused on psychological situation of all study individuals when sample collection ,and the blood sample used to measured cortisol ,HbA1c and cystatin c levels

Results: This study shows elevation of serum Cystatin C level , serum cortisol level and HbA1c in un-control DM (with DN) group compare with control DM (without DN) group

Conclusion: This study confirms that depression can cause elevation of cortiaol level that lead to increase HbA1c level to result un-control DM , that cause early stage of DN . DN detect by elevation of cystatin C level

Keywords: Diabetes Mellitus, Diabetic Nephropathy, Serum Cortisol Level , Serum Cystatin C Level

Introduction

Diabetic Nephropathy (DN) is disorder occur in renal nephrons caused by diabetes mellitus (DM) disease , therefore the DN consider is the most important of micro vascular complication of DM . DN can lead to many morphological and functional changes , for example elevation of urinary albumin and glomerular basement membrane density due to

nephron's tissue damage (1) . In end state of renal disease the most patients need to dialysis or renal transplantation ,also the most DN patients suffer of hypertension , myocardial infraction and other complications that cause mortality . Several previous study shown that elevation of serum glucose level for short period (control DM) can't cause nephron's tissue damage , but serum glucose level for long period (un-control DM) can cause nephron's tissue damage (DN) .Therefore un-control DM consider as high risk factor for developed renal disease , the un-control DM detection by high glycated hemoglobin (HbA1c) level for long periods (2) .

Cystatin C is monomeric and non-glycosylated protein encoder and product by *cst3* gene that occur on chromosome 20 (3) . it has many role in body such as cysteine proteinases inhibitors of papain family (C1) and inhibition of microbial cysteine proteinases in blood .Cystatin C has many roles in human body such as diagnosis role in renal, heart and neurology diseases (4) .

Cortisol is the most important stress hormone ,it's release from adrenal cortex layer to all cells by blood .The functions of cortisol in cells include: regulation of blood sugar levels, metabolic process , anti-inflammatory, and other functions .The release of cortisol hormone regulation by sympathetic nervous system that effect by various types of stress (5) . Stress is a situation caused by various factors and characterized by an imbalance in body functioning, impair in the nervous system and tension . The stress effect on cortisol release via stress sensitive endocrine response systems that classify into hypothalamic–pituitary–adrenal (HPA) axis and sympathetic adrenal medullary system. Also must be know that cortisol level reach to high level at morning then fall at evening time (6) .

Materials and Methods

The present study included 40 DM cases group classified into 20 control DM (without DN) and 20 un-control DM (with DN) ,all cases diagnosis by KDIGO 2020 (Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease). All subjects age in current study was more than 50 years of both genders , this study was done in Al-Yarmouk Teaching Hospital – Iraq .The current study focused on psychological situation of all study individuals when sample collection .The blood samples separated into 2 tubes after drawing , the first tube treated with EDTA for measured HbA1c (by chromatography method) ,and the second tube immediately separated by centrifuge after draw from all individual to obtain pure serum to measure serum Cystatin C level (by

immunoassay method) and serum cortisol levels in P.M. period (by TOSOH instrument) .

The results statistic analysis in this study was used the t-test method to show different in HbA1c , cystatin C and cortisol level between un-control DM (with DN) and control DM (without DN) groups. The t-test method used mean \pm standard deviation (SD) and p-value ($>$ 0.05 significant value) .

Results

This study compared between 2 groups un-control DM (with DN) and control DM (without DN) at three parameters serum cortisol level , HbA1c and serum Cystatin C level , to know the different in these levels between two groups . Theses result show clinical significant different between all parameters included in this study between groups . .Show table 1.

Table 1: Comparison of serum cortisol level , HbA1c and serum Cystatin C level between Control DM (without DN)and Un-control DM (with DN) groups according to mean \pm standard deviation (SD)

Parameters level	Control DM (without DN) group	Un-control DM (with DN) group	P-value
Cortisol (ng/ml)	6.5 \pm 0.96	9.2 \pm 1.1	0.012
HbA1c (%)	7.1 \pm 0.81	9.8 \pm 1.3	0.017
Cystatin C (mg/L)	2.01 \pm 0.50	3.31 \pm 2.00	0.020

Discussion

Diabetic Nephropathy (DN) is the most important of diabetes mellitus (DM) disease complications about micro vascular level that it refer to primary kidney disorder .DM is chronic disease has many harmful effects on human body for example retinopathy , diabetic foot and DN , these effects cant lead to worry feeling , also called psychiatric stress (1) . The psychiatric stress of DM patients can convert to depression if the worry feeling of patient become high , this situation lead to stimulate primary stress hormone secretion ,commonly cortisol hormone (7) .

The cortisol hormone is release by adrenal gland at diurnal cycle style , elevation at a.m. period and reduce at p.m. period , and has many functions in human body like regulation of bio-molecular metabolisms and other functions , so the cortisol hormone act to stimulate glycogenolysis and gluconeogenesis process in muscle and liver (5) . Glycogenolysis and gluconeogenesis are metabolic processes lead to increase of serum glucose level that can development of DM severity then lead to un-control serum glucose level , on the long period lead to elevation of HbA1c percent , in this situation the patient become un-control DM patients (8) .

Elevation of serum glucose level can cause various complications in human body if it elevated for long time such as nephron tissue damage that lead to impair nephron functions . The failure nephron function coupled with reduce of glomerular filtration rate (GFR) , therefore used serum Cystatin C level to detection of GFR reduction that refer to renal vascular injury at early stage of renal failure (9)

Cystatin C is more specific and sensitive to kidney function due to Cystatin C is protein has many function in human body and it can pass from glomerular filtration membrane as free , also it can complete re-absorption in proximal tubule cells but not back to blood cycle and the renal can't secrete it (3) .

The present study results shown increase of serum cortisol level in un-control DM (with DN) group compared with control DM (without DN) group ,these increase can stimulated by psychiatric stress (depression) of patients . This results agree with Psarraki EE, and et al 2020 that documented linear correlation between depression and serum cortisol level (10) . Also this study results confirm elevation of HbA1c by effect of serum cortisol level increase , that agree with results of Johar H, and et al 2021 (11) .Then this study show elevation of serum cystatin C level in un-control DM (with DN) group that agree with Guo JJ, and et al 2017 (12) also agree with (Kachhawa K, and et al 2016 (13) that confirmed serum Cystatin C level can used as early marker for assessment of kidney function in patients with DN disease .

Conclusion

The study results concluded elevation of serum cortisol level by depression (increase of cortisol secretion) in un-control DM (with DN) patients , high cortisol lead to increase of HbA1c that refer to high serum glucose level for long periods , this lead to fail of nephron function (DN)

(decrease of GFR) that detected by serum cystatin C level increase at early stage

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