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OXIDATIVE STRESS ASSESSMENT IN PATIENTS WITH DIABETIC NEPHROPATHY

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ABSTRACT

It is well known that diabetes mellitus is one of the diseases that is associated with oxidative stress and antioxidant mechanism. This study was done to measure and analyze the serum levels of total oxidant and total antioxidant parameters in patients with diabetic nephropathy. A study was done on 45 patients (25 males and 20 females), aged (50 years ±8) with diabetic nephropathy disease and 50 healthy subjects (28 males and 22 females), aged (48 years± 5). Blood level of hemoglobin A_{1C} percent as well serum levels of reactive oxygen metabolites and total antioxidant status were measured and studied. The statistical results for patients with diabetic nephropathy offered high momentous increase ($P<0.001$) in blood level of hemoglobin A_{1C} percent as well in serum level of reactive oxygen metabolites when compared with control healthy subjects. Conversely, in contrast to control subjects, the patients with diabetic nephropathy revealed high considerable decrease ($P<0.001$) in serum level of total antioxidant status. On Inferences, these observation on patients with diabetic nephropathy, demonstrated the degree of imbalance between oxidative and ant oxidative statuses that may be related to clinical events and complication accompanied diabetic nephropathy.

KEYWORDS: Diabetic nephropathy, reactive oxygen metabolites, Total antioxidant status.

INTRODUCTION

Oxidative stress is a state that related to the complication of many diseases. It is occurs as a result of serious imbalance between oxidants and antioxidants statuses within the tissues of the body causing damage of the cellular component that include proteins, lipids and DNA.[1]

The checking of oxidative state inside the body is done either by measuring the products of oxidative damage or by analyzing the capacity of the body fluid to endure extra oxidation. Whereas the examining of antioxidant state is done either by measuring the particular components of antioxidant or by analyzing the entire reducing activity of the body fluid which reflect its total antioxidant efficacy.[2]

Oxidative stress is a well-established feature of diabetes mellitus and is believed to play an important role in the development of diabetes-related complications.[3] hemoglobin A_{1C} percent (HbA1c %) is a recommended biomarker for diabetes diagnosis and monitoring.[4] Compared to fasting glucose test or glucose tolerance test, HbA1c % has the advantage of convenience and free from acute perturbations.[5]

The principle of this study was to measure the blood level of hemoglobin A1C percent (HbA1c %) as well the serum levels of reactive oxygen metabolites (ROM) and total antioxidant status (TAS) in a group of patients with diabetic nephropathy, thereafter to assess their association with the imperil of diabetes in reference to healthy subjects.

PATIENTS AND METHODS

Forty five patients,(25 males,20 females), aged (50 years ±8) with diabetic nephropathy and 50 control subjects (28 males, 22 females) aged (48 years ±5) enrolled from Al- yarmouk hospital.

Criterions of inclusion made based on clinical symptoms and biochemical tests while criterions of exclusion are involved patients with liver disease, heart failure and patients with estimated glomerular filtration rate (eGFR) equal to 15 ml/min/1.73m^2 or patients under dialysis.

The levels of HbA1c % are measured on fasting blood samples as well as the serum samples are used to measure the levels of the reactive oxygen metabolites (ROM) and the total antioxidant status (TAS) by using commercial tests kits with Photometric Colorimetric method.[6,7,8]

All eligible participants offered written informed consent to partake in this study. The study protocol conforms to

the ethical guidelines and endorsed by the institution's ethics committee.

Statistical results are displayed as average (mean) ± standard deviation (SD) with 95% confidence interval (CI) and *P* values of equal to or less than 0.05 were reckoned statistically significant. All statistical analyses were performing using series SPSS version 18.

RESULTS

The details and the statistical results of the data of the studied groups are presented in Table 1.

Notably, high powerful increases (P<0.001) were showed in average level of blood Hb_{A1C} % and in average level of serum ROM for patients with diabetic nephropathy as compared with control healthy subjects.

Conversely, in contrast to control subjects, high powerful decrease (P<0.001) was noted in average level of serum TAS for patients with diabetic nephropathy.

Concerning the percentage changes of the patient's variables as compared to their control levels, the blood Hb_{A1C} % ratio was elevated more than the serum ROM ratio, while the serum TAS ratio suppress by a value that is in between Hb_{A1C} % ratio and ROM ratio but in opposite direction as shown in Fig.1.

The power analysis for the minimum detectable change percent (MDC %) between the average levels of control variables and the average levels of patients variables for Hb_{A1C} %, TAS and ROM are elucidated in Fig. 2.

Table 1: Statistical outlines for clinical data and demographic characteristics of the studied groups.

Variables	Control	Patients
Number(male, female)	50 (28,22)	45 (25,20)
Age(years)	48 ± 5	50 ± 8
Hb_{A1C} %	6.5 ± 0.8	8.6 ± 0.7 ***
ROM (CARRU)	383 ± 46	492.2 ± 60 ***
TAS (µmol/L)	1500 ±110	1048.5 ± 85 ***

*Data are presented as mean ± SD for continuous variable, *** = high significant difference P<0.001 vs. control.*

***Abbreviation**: Number: Sample size of the participants, ROM: reactive oxygen metabolites, TAS: total antioxidant status Hb_{A1C} %; Hemoglobin A1C percent, One CARR U = 0.08 mg/100 mL H_2O_2, TAS (µmol/L)= micro mole of Trolox Equivalent/liter, Trolox Equivalent; vitamin E analog.*

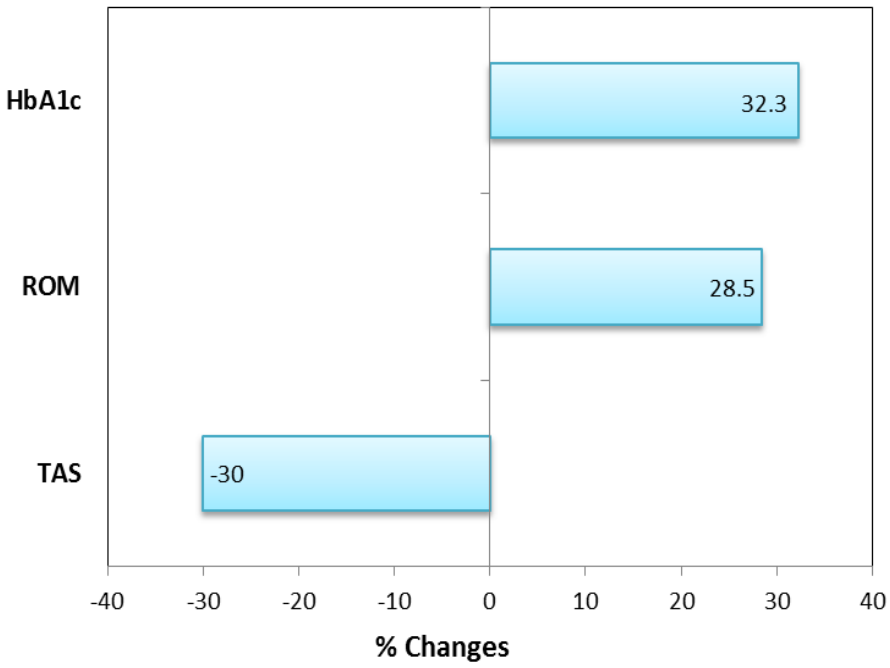

Fig. 1: Bar graph elucidated the percentage changes in mean level of blood hemoglobin A1C percent (Hb_{A1C} %) and in mean levels of serum total antioxidant status (TAS) and serum reactive oxygen metabolites (ROM) for patients with diabetic nephropathy as compared with their control levels.(Sample size (n)=50 for control subjects, (n)=45 for patients with diabetic nephropathy).

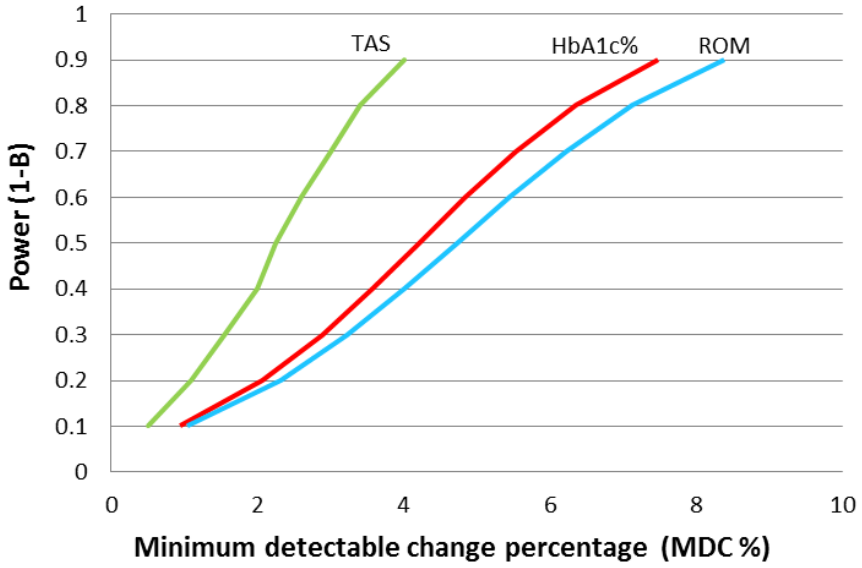

Fig. 2: Power analysis for the minimum detectable change percent (MDC %) between the mean levels of control and diabetic patients for hemoglobin $_{A1C}$ % ($Hb_{A1C\%}$), total antioxidant status (TAS) and reactive oxygen metabolites (ROM). Assuming alpha =0.05 and power = 80%. Sample size (n)=50 for control subjects, (n)=45 for patients with diabetic nephropathy.

DISCUSSION

Oxidative stress is one of the most important reasons for the advance complication of the diabetes mellitus.[9,10] The elevated blood level of glucose for long time leading to the production of free radical and thereafter formation of advanced glycated end products (AGE).[11] The free radicals cannot measure directly in serum or plasma fluid because of their short half-life. Therefore, other markers employed to assess the oxidative and ant oxidative status.

The measuring of total antioxidant efficacy of the body fluid like plasma is more preferable than measuring single antioxidant species because it's obviously reflect the in vivo balance between all types of oxidizing agents and antioxidant agents whether they are known or unknown, measurable or immeasurable.[12]

In this study, different markers used to evaluate the oxidative status of the patients with diabetic nephropathy in addition to commonly used marker, Hb_{A1C} %. Along with the below studies and as compared to control level, the statistical results illustrated that the diabetic nephropathy is associated with the appreciably increase in oxidative stress marker (ROM) and glycated hemoglobin percent (Hb_{A1C} %). Conversely, a considerably decrease in total antioxidant status marker (TAS) have been noted.

Although some study stated that ROM test measured only ceruloplasmin oxidase level but it is reflected the actual status of oxidative stress.[13] Other studies mentioned that the level of the ceruloplasmin oxidase does not reflect the accurate status of oxidative stress.[14,15,16]

Concerning the level of TAS, Pinaki *et al*, in 2015 revealed that the level of fasting blood glucose is well associated with TAS in diabetic patients.[17] It is noteworthy that the TAS test is not specific for a particular antioxidant species but it is used to assay the overall antioxidants species.[8]

CONCLUSIONS

These observation on patients with diabetic nephropathy, illustrated and suggested that another markers like total antioxidant status or reactive oxygen metabolites can be used to precisely monitor the oxidative status of the patients with or without Hb_{A1C}% measurement.

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