

## Association of Oxidative Stress and Psychological Stress in Hypertensive and Normotensive Diabetes Patients

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DOI: [10.36347/sjams.2019.v07i07.046](https://doi.org/10.36347/sjams.2019.v07i07.046)

| Received: 05.06.2019 | Accepted: 12.06.2019 | Published: 30.07.2019

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### Abstract

### Original Research Article

**Objectives:** Diabetes is a metabolic disease which hosts plethora of disease conditions. Among which is hypertension is the key initiating the cascade of metabolic derangements. Blood pressure impairs the metabolic functions and even leads to inviting high free radicals (reactive species). Alongside, increase in psychological stress occurs too aggravating the situation which may be borne out of diabetic conditions or others environmental elements. **Methods:** We collected blood samples from 100 diabetic patients and 50 controls. Serum levels of malondialdehyde and cortisol were measured by ultraviolet spectrophotometry and enzyme-linked immunosorbent assay kit, respectively. **Results:** We found serum total-antioxidant, malondialdehyde and cortisol levels of both the hypertensive and normotensive diabetes patients significantly higher than their healthy counter parts. **Conclusion:** The present study showed that increased serum levels of malondialdehyde and cortisol are strongly associated with diabetes but not with each other. Therefore, we believe elevations of malondialdehyde and cortisol in serum level arise independently and they could serve as biomarkers for diabetic patients.

**Keywords:** Hypertension, malondialdehyde, cortisol, anti-oxidant.

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## INTRODUCTION

Ever burgeoning cases of metabolic diseases has threatened people lives and also put forth extremely daunting situation to the medical field. Almost all the adult not sparing the younger ages, having been victimized by this perilous experience which has triggered mass awareness among people, who are vigorously opting green and clean life style modifications as an endorsement. Despite this, metabolic disease like diabetes mellitus (DM) characterized by hyperglycemia, hypertension, deranged lipid profile and more seems not to retreat. Basically, this metabolic disorder are borne out of abnormal metabolism of macronutrients such as carbohydrate, protein and fat [1-4]. Un-healthy high calorie diet accompanied by sedentary life styles engenders high blood pressure, hyperglycemia and cholesterol which generates reactive oxygen species (ROS), in other hand, depresses the activity of free

radical scavengers, which in turn cause damage to the cells in many ways. Damage to the cells ultimately results in secondary complications in diabetes mellitus. Studies have shown various health issues like high blood pressure, high blood sugar level, low HDL and high LDL [5-7]. In spite, of many years of research in diabetes, it is still unknown, what is the genetic premise for hypertension. For sure, there is intricate connection of genes and environmental attributes [8-10]. Furthermore, it has been clearly grasped as of how smoking, drinking, inactive life, obesity and ongoing stress aggravate the cardiovascular complications [11-15]. Among myriads of variables that can lead to high blood pressure oxidative stress is invariably at the top as it results in endothelial dysfunction. Similarly, reactive oxygen species can be linked to hyperglycemia as well. The rise in blood sugar level has been speculated to be due to presence of anti-insulin hormones like glucagon, epinephrine, glucocorticoids

etc. or possibly due elevation of various cytokines such as TNF- $\alpha$  and IL-1. Thus, one can anticipate that ongoing day to day stress as well as un-hygienic life style can increase the severity and accentuate the prevalence of diabetes in the community. Thus this study aims to study level of anti-oxidant, extent of oxidative stress and psychological distress level and their correlation with each other under normotensive and hypertensive diabetic conditions.

## MATERIALS AND METHOD

The present study was carried out in the Departments of Biochemistry and in the Department of Medicine, Rama Medical College, Hospital and Research Center, Pilakhuwa, Hapur.

### Sample Size

Total number of 100 patients of Diabetes of either sex (age 30-75 years) were included in the study from the OPD and IPD of RAMA Hospital. These were divided into two groups on the basis of their Systolic/Diastolic Blood pressure. 50 healthy subjects were also included in the study from employee of departments, friends and their relatives as control. Serum levels of malondialdehyde and cortisol were measured by ultraviolet spectrophotometry and enzyme-linked immunosorbent assay kit, respectively.

## RESULT AND OBSERVATION

**Study Design:** A case control study.

**Duration of research:** 01-10-2018 to 1-04-2019 (six months)

### Inclusion Criteria

All pre-diagnosed Normotensive and Hypertensive Diabetic patients will be included as per the American Diabetes Association criteria(ADA, 2016) 77 and Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure(JNC 7th Edition) criteria[16]. Diabetic patients in the age group 30-75 years (either sex).

### Exclusion Criteria

Only hypertensive patients i.e. without Diabetes, Gestational diabetic patients, Other chronic complications related to DM, Secondary diseases like thyroid dysfunction, Organ transplanted diabetic patients, Other chronic illness like HIV, Cancer, TB ,Age: < 20 years & >75 years, Pregnant women.

## STATISTICAL ANALYSIS

The observed data was tabulated, processed and statistically analyzed via IBM SPSS Statistics version 21

**Table-1: Demographic profile of study group subjects (Mean  $\pm$  SD)**

Parameters	Healthy controls	Normotensive	Hypertensive
No. of samples	50	59	41
Male/Female ratio	43/7	31/28	21/20
Age	43.16 $\pm$ 3.17	47.1 $\pm$ 6.2*	52.15 $\pm$ 7.0*
SBP (mmHg)	114.16 $\pm$ 3.84	116.78 $\pm$ 3.61*	145.83 $\pm$ 4.32*
DBP(mmHg)	74.84 $\pm$ 4.92	76.32 $\pm$ 3.16*	93.07 $\pm$ 5.16*
Disease duration of Diabetes (years)	-	6.78 $\pm$ 3.3	7.24 $\pm$ 4.0

Where, \*\* p<0.001: Statistically significant and \* p>0.05: Statistically non-significant

**Table-2: Parameters of oxidative and psychological stress in diabetes**

Particulars	Healthy controls	Normotensive	Hypertensive
Fasting Blood Sugar (mg/dl)	83.25 $\pm$ 11.17	181.59 $\pm$ 20.66***	167.44 $\pm$ 17.81***
Malondialdehyde ( $\mu$ mole MDA/ml)	2.80 $\pm$ 0.35	3.07 $\pm$ 0.54***	4.02 $\pm$ 0.73***
Total antioxidant capacity, FRAP ( $\mu$ M)	4.77 $\pm$ 1.38	3.20 $\pm$ 1.49***	2.56 $\pm$ 1.51***
Cortisol (n mole/L)	284.28 $\pm$ 36.51	425.62 $\pm$ 40.44**	650.20 $\pm$ 52.14**

Where, \*\*\* p < 0.001: Statistically highly significant, \*\* p < 0.05: Statistically significant  
\* p > 0.05 : Statistically non-significant

**Table-3: Correlation of cortisol and MDA under normotensive and hypertensive conditions**

Particulars	Healthy Control	Normotensive	Hypertensive
Psychological stress (Cortisol)	Oxidative stress(MDA)		
R value	0.42*	-0.142*	0.249*

\* p > 0.05 : Statistically non-significant

## DISCUSSION

In the whole, studied group showed statistically significant association of plasma total antioxidant capacity (FRAP, p-value <0.001) and oxidative stress marker (MDA, p-value <0.001) between patients and the (p-value <0.001) control groups was found, which was similar to the findings from various other studies[17-20], which confirms that the level of antioxidant capacity (FRAP) is decreased and the oxidative stress status measured as MDA in the case of diabetes (hypertensive and normotensive) patients in comparison with the control subjects, i.e. the oxidant stress is increased in patients with hypertension and diabetes as in similar to other study[12, 21-25]. In the study, a similar significant increase in MDA levels ( $p < 0.05$ ) and decrease ( $p < 0.05$ ) in FRAP levels were found when compared to controls.

Known fact of life long management and poor prognosis is upsetting and adds on to further psychological distress. Thus, secretions of stress hormone, cortisol rises. Our study showed statistically highly significant increase levels of the cortisol hormone in patients when compared to control subjects (<0.001), similar findings have been reported in previous studies [27, 28] in diabetes patient and control group respectively. However, the association between cortisol and MDA was found in-significant in our study, no exact study was found to correlate, but one study where MDA had highly negative relation with cortisol in major depressive patient was found [28].

## CONCLUSION

The present study suggested that increased serum levels of malondialdehyde and cortisol in hypertensive and non-hypertensive diabetes patient are far from co-relation. We believe elevations of malondialdehyde and cortisol in serum level arise independently and they could serve as independent biomarkers for oxidative stress and psychological stress.

## REFERENCES

1. Marshall SM, Flyvbjerg A. Clinical review- Prevention and early detection of vascular complications of diabetes. *BMJ-British Medical Journal-International Edition*. 2006;333(7566):475-80
2. Ramachandran A, Snehalatha C. Current scenario of diabetes in India. *Journal of diabetes*. 2009;1(1):18-28.
3. Mellitus D. Diagnosis and classification of diabetes mellitus. *Diabetes care*. 2005; 28:S37.
4. TAS. Diagnosis and classification of diabetes mellitus. *Diabetes care*. 2014; 37:S81.
5. Hunt JV, Dean RT, Wolff SP. Hydroxyl radical production and autoxidative glycosylation. Glucose autoxidation as the cause of protein damage in the experimental glycation model of diabetes mellitus and ageing. *Biochemical journal*. 1988;256(1):205-12
6. Jaganjac M, Tirosh O, Cohen G, Sasson S, Zarkovic N. Reactive aldehydes—second messengers of free radicals in diabetes mellitus. *Free Radical Research*. 2013;47(sup1):39-48.
7. [https://en.wikipedia.org/wiki/Hypertension#cite\\_note-JNC8](https://en.wikipedia.org/wiki/Hypertension#cite_note-JNC8)
8. <https://en.wikipedia.org/wiki/Hypertension#Diagnosis>.
9. Studies ICfBPG-WA. Genetic variants in novel pathways influence blood pressure and cardiovascular disease risk. *Nature*. 2011;478(7367):103-9.
10. Lifton RP, Gharavi AG, Geller DS. Molecular mechanisms of human hypertension. *Cell*. 2001 Feb 23;104(4):545-56.
11. Álvarez MF, Alzate AV, Campos CA, Giraldo MF, Hachito J, Mesa IC, Rojas CA, Rodríguez-Valois D, Castaño-Castrillón JJ, Giraldo JF. Exploración inicial de los valores de tensión arterial y factores de riesgo asociados a hipertensión arterial en estudiantes de la Universidad de Manizales, Colombia en el 2009. *Revista Médica UIS*. 2010 Dec 14;23(3).
12. Paravicini TM, Touyz RM. Redox signaling in hypertension. *Cardiovascular research*. 2006;71(2):247-58.
13. Papathanasiou G, Zerva E, Zacharis I, Papandreou M, Papageorgiou E, Tzima C, Georgakopoulos D, Evangelou A. Association of high blood pressure with body mass index, smoking and physical activity in healthy young adults. *The open cardiovascular medicine journal*. 2015;9:5.
14. Forbes JM, Coughlan MT, Cooper ME. Oxidative stress as a major culprit in kidney disease in diabetes. *Diabetes*. 2008;57(6):1446-54.
15. Huang PL. eNOS, metabolic syndrome and cardiovascular disease. *Trends in Endocrinology & Metabolism*. 2009 Aug 1;20(6):295-302.
16. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo Jr JL, Jones DW, Materson BJ, Oparil S, Wright Jr JT, Roccella EJ. Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. *hypertension*. 2003 Dec 1;42(6):1206-52.
17. Lamichhane A, Prasad S, Bhaskar N, Singh J, Pandey R. Malondialdehyde (MDA): an oxidative stress marker in type II Diabetes mellitus with and without complications. *Current Trends in Biotechnology and Chemical Research*. 2013;2(2):110-2.
18. Kshitiz K, Varun SK, Ranjan A, Kesari J. Study of serum malondialdehyde and vitamin C status in type 2 diabetes mellitus. *Int J Curr Res Acad Rev*. 2015;3(4):20-5.
19. Mohamed EI, Elazomi A, Elabid BEH, Zwaik H. Evaluation of Changes in Levels of plasma MDA,

- and Antioxidant Vitamin E in Sudanese patients with type2 Diabetes. Age (years). 2014;55(12.41):23.00-86.00.
20. Amanullah M, Zaman GS, Rahman J, Rahman SS. Lipid peroxidation the levels of antioxidant enzymes in hypertension. Free Radicals and Antioxidants. 2012;2(2):12-8.
  21. Hirata Y, Satonaka H. Hypertension and oxidative stress. Japan Medical Association Journal. 2001;44(12):540-5.
  22. Ramakrishna V, Jaikhani R. Oxidative stress in non-insulin-dependent diabetes mellitus (NIDDM) patients. Acta diabetologica. 2008;45(1):41-6.
  23. Kaur K, Bedi G, Kaur M, Vij A, Kaur I. Lipid peroxidation and the levels of antioxidant enzymes in coronary artery disease. Indian journal of clinical biochemistry. 2008;23(1):33-7.
  24. Arora M, Mahat RK, Kumar S, Tyagi S, Batra J. Oxidative stress and its relation to glycemic control in patients of type 2 diabetes mellitus. International Journal of Medical Science and Public Health. 2016;5(6):1173-7.
  25. Alam R, Khan S, Salman KA. MDA and Antioxidants Status in Type 2 Diabetes Mellitus. National Journal of Integrated Research in Medicine. 2013 Nov 1;4(6).
  26. Chiodini I, Adda G, Scillitani A, Coletti F, Morelli V, Di Lembo S, Epaminonda P, Masserini B, Beck-Peccoz P, Orsi E, Ambrosi B. Cortisol secretion in patients with type 2 diabetes: relationship with chronic complications. Diabetes care. 2007 Jan 1;30(1):83-8.
  27. Hakkarainen P, Moilanen L, Hänninen V, Heikkinen J, Räsänen K. Work-related diabetes distress among Finnish workers with type 1 diabetes: a national cross-sectional survey. Journal of Occupational Medicine and Toxicology. 2016;11(1):11
  28. Islam MR, Islam MR, Ahmed I, Moktadir AA, Nahar Z, Islam MS, Shahid SF, Islam SN, Islam MS, Hasnat A. Elevated serum levels of malondialdehyde and cortisol are associated with major depressive disorder: A case-control study. SAGE open medicine. 2018 May 8;6:2050312118773953.