

## Study of levels of vit-C, albumin and uric acid as a component of total antioxidants defens system in type- 2 diabetic patient

\*Anwar j. TH. AL- Mazaal

### Abstract

This study was carried out in 38 hospitalized patients with uncontrolled type 2 diabetes mellitus and in 38 apparently healthy individual to assess the changes in antioxidants (vit -C, albumin, uric acid) as component of total antioxidant defense system . The results showed a marked reduced significantly ( $P < 0.01$ ) in levels of (vit - C, albumin) and significant increased ( $P < 0.05$ ) in levels of uric acid in uncontrolled type 2 diabetes , as in healthy individual. Though good control of blood glucose with antioxidant therapy could help in reducing free radical activity and minimize major complications in diabetic patients. In diabetes, the persistence of hyperglycemia has been reported to cause increased production of oxygen free radicals through glucose autooxidation and nonenzymatic glycation. The aim of this study was to determine the changes in antioxidants like ( vit - C, albumin, uric acid) as component of total antioxidant defense system in type 2 diabetic patients.

### الخلاصة

تم دراسة (38) مريض من النوع الثاني من داء السكري و(38) من الأصحاء كمجموعة سيطرة حيث تم قياس مستويات مضادات الاكسدة ( فيتامين - سي ، اليومين ، وحمض اليوريك ) كاحد مكونات النظام الدفاعي. وقد اظهرت النتائج انخفاض مهم ( $P < 0.01$ ) في مستويات فيتامين - سي والاليومين وارتفاع في مستويات حمض اليوريك لدى مرضى السكري من النوع الثاني بالمقارنة مع مجموعة السيطرة.

### Introduction

Antioxidants can be defined as any substances that when present in low concentration compared to those of an oxidizable substrate , significantly delay or inhibit oxidation of that substrate <sup>(1)</sup> . The antioxidant defense system of the body has many components including metal binding proteins such as transferrin, ferritin , ceruplasmin and albumin , which are considered as a primary antioxidant . These binding proteins work by reducing the availability of metal ions which play an important role in free radical formation . Also there are enzymatic antioxidants as superoxide dismutase (SOD) catalase(CAT) and nonenzymatic antioxidant defense systems involving small molecules such as vit-C ,vit-E ,uric acid and bilirubin these act to scavenge free radicals and prevent them taking part in reactions which could cause cell damage .A deficiency in any of these components can cause a reduction in the overall or total antioxidant status (TAS) of an individual <sup>(2)</sup> . Total antioxidant status may be used as an important tool for screening the identification of risk factors

\*Biochemistry Departement- College of Medicine  
University of AL- Qadisiya.



in patients and as monitoring tool for assessing the effect of drug treatment regimes<sup>(5)</sup> (TAS) measure the contribution to plasma antioxidants like enzymes, proteins, and small molecules like uric acid<sup>(4)</sup>. In diabetes, the persistence of hyperglycemia has been reported to cause increased production of oxygen free radicals through glucose autoxidation and nonenzymatic glycation. The measurement of antioxidants in type 2 diabetic patients is thus a useful indicator of risk from diseases associated with free radicals activity, and may indicated the need for antioxidant therapy<sup>(4)</sup>.

### **Materials and methods**

Thirty – eight patients (28 men and 10 women) were included in the study. Their mean age was  $(50 \pm 1)$  years (range 40 to 60 years). All had attended to Al- Dywania teaching hospital for follow – up clinics over one month period and all fulfilled the following three criteria (Fasting plasma glucose  $(\leq 550$  mg / 100 ml)

patient as compared with control group ( $0.385 \pm 0.041$ ). A significantly decreased ( $p < 0.01$ ) in serum albumin concentration ( $2.8 \pm 0.59$ ) has been shown in Fig (2) in diabetic patient than control group ( $4.33 \pm 0.66$ ). Serum uric acid levels were significantly increase ( $P < 0.05$ ) in diabetic patients ( $107.15 \pm 19.93$ ) as Compared with control group ( $61.88 \pm 16.74$ ) Fig (3). (FSG) concentration was inversely and significantly related with serum vit- C concentration ( $r = - 0.613$ ) ( $P < 0.05$ ) Fig (4). It was also inversely and significantly related with serum albumin concentration ( $r = - 0.419$ ) ( $P < 0.05$ ) Fig(5). while the correlation between serum uric acid levels and (FSG) was found non significant ( $r = -0.22$ ) ( $P = 0.08$ ).

**Table (1)** The mean and standard deviation of variables (glucose, Vit - C, uric acid, albumin,) in both type 2 diabetic

Parameter	Patients and control		P - value	Groups
	Control n=38	Patients n=38		
	88.28 ± 5.54	230.57 ± 111.31	< 0.01	FSG
Vit - C (mg /100ml)		0.385 ± 0.041	0.255 ± 0.05	< 0.01
Uric acid (mg /L )		61.88 ± 16.74	98.15 ± 19.93	< 0.05
Albumin (g / 100 ml)		4.33 ± 0.66	2.8 ± 0.59	< 0.01



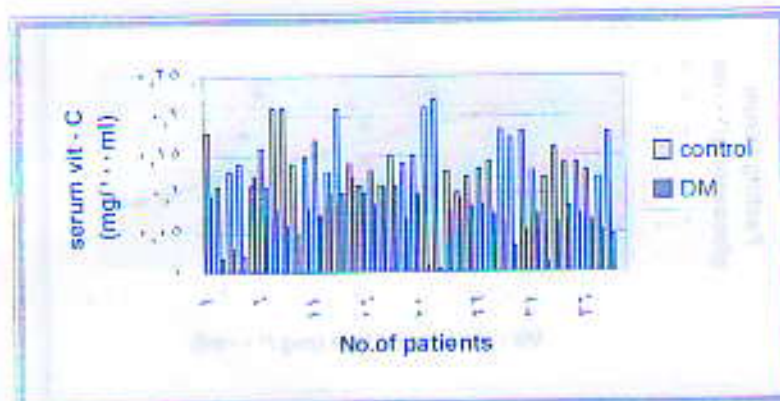


Fig (1) the mean and standard deviation of serum vit - C in type 2 Diabetic patients (DM) (n =38) and control (n = 38).

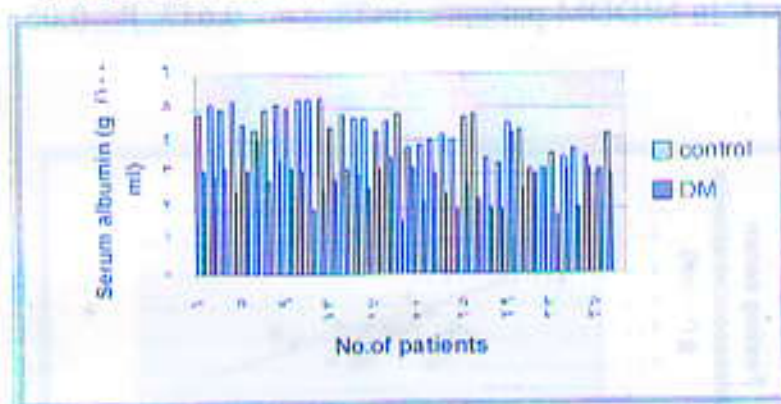


Fig (2) the mean and standard deviation of serum albumin in type 2 Diabetic patients (DM) (n = 38) and control (n = 38).

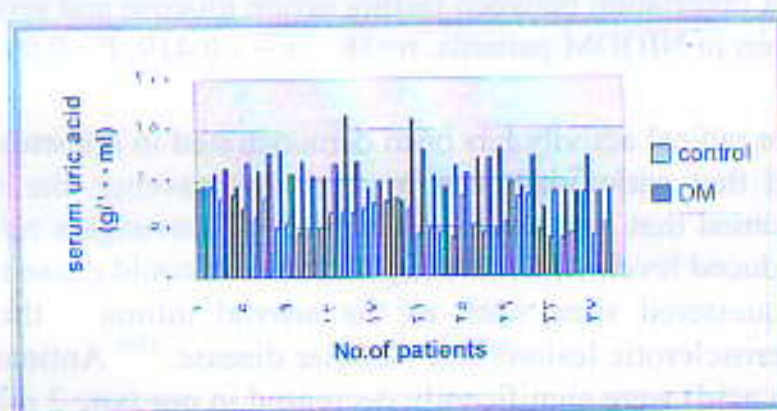


Fig (3) the mean and standard deviation (serum uric acid in type 2 Diabetic patients (DM) (n =38) and control (n=38).

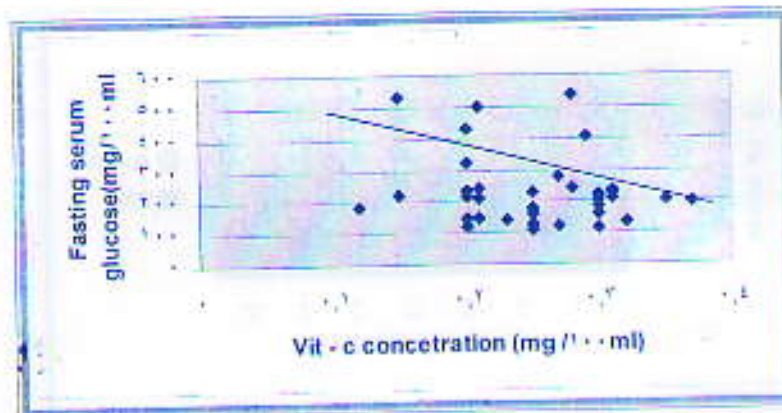


Fig (4) A correlation between fasting serum glucose and serum Vit - C in NIDDM patients.  $n=38$ ,  $r = - 0.613$ ,  $P < 0.05$

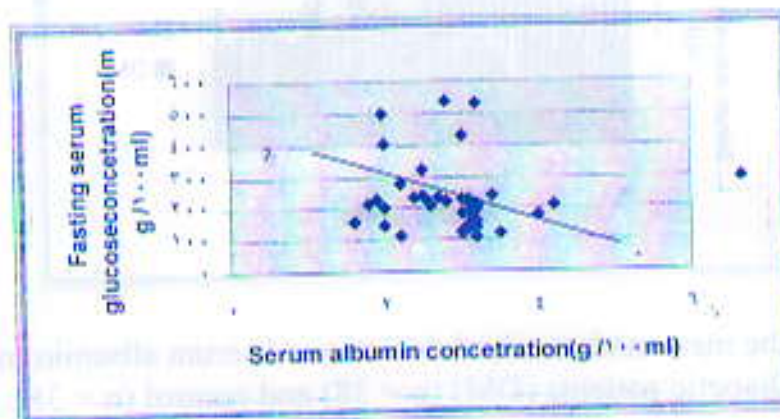


Fig (5) A correlation between fasting serum glucose and serum albumin in NIDDM patients.  $n=38$ ,  $r = - 0.419$ ,  $P < 0.05$

## Discussion

Increased free radical activity has been demonstrated in diabetes mellitus<sup>(9)</sup>. It has been suggested that antioxidant can be used to scavenge the increased free radicals. It was assumed that low levels of free radical scavengers reflect increased oxidative stress. Reduced levels of circulating antioxidant could cause increased lipid peroxidation in sequestered sites, such as the arterial intima this favours the development of atherosclerotic lesions and vascular disease.<sup>(10)</sup> Antioxidants such as (vit C, albumin, uric acid) were significantly decreased in our type 2 diabetic patients. These findings suggest the existence of low antioxidant defense in these patients, which may be due to:

- lower dietary intake of antioxidants such vitamins A, C and E and sulphur containing amino acids such as methionine in the diet.
- More utilization of these antioxidants to remove excess free radicals produced by diabetes mellitus<sup>(9)</sup> other sources could include auto-oxidation of glucose<sup>(11)</sup> and non enzymatic glucation<sup>(12)</sup>. In diabetes plasma glucose is high and there are more



chances of excess free radicals production, causing significant decrease in total antioxidant status<sup>(4)</sup>. Our results for diabetic patients appeared to support most previous studies in finding that persons with diabetes mellitus have lower serum vitamin C concentration than that without diabetes ( $P < 0.01$ ) Fig(1).<sup>(23)</sup>

reviewed previously only 7 found that blood vitamin C concentration not significantly lower in diabetic persons than concentration in persons without diabetes<sup>(13)</sup> Several explanations for reduced serum vit - C concentration in persons with diabetes might considered:

- 1- Renal reabsorption of vitamin C may be reduced by hyperglycemia .
- 2- Blood glucose may compete with vitamin C for uptake into certain cells and tissues.
- 3- Cellular regulation of vitamin C may be impaired.
- 4- Increased oxidative stress may deplete antioxidant reserves.

This study suggests that increasing antioxidant protection against free radicals may possibly reduce complications in type-2 diabetic patients. Indeed ,antioxidant supplements such as vitamins A,C and E may achieve these aims<sup>(14)</sup> good controls of plasma glucose in type 2 diabetic patient could also reduce free radicals activity and the risk of complication<sup>(15)</sup> Our results for type 2 diabetic patients show that low serum albumin concentration associated with diabetes( $P < 0.01$ ) Fig(2). Poorly controlled diabetes is associated with altered body metabolism<sup>(16)</sup> Insulin – mediated net protein anabolism occurs largely in skeletal muscle wasting<sup>(17)</sup>. Similarly decreased synthesis of hepatic plasma protein (eg. albumin) has been show in diabetes<sup>(16, 18)</sup> low serum albumin concentration were associated with diabetes. The treatment of diabetes with insulin ,greater energy intake,and inflammation were associated with low serum albumin concentration<sup>(19)</sup> similar associations between diabetes and low serum albumin were found by using data derived from NHANES<sup>(20)</sup>. These findings suggest the twice risk of low serum albumin concentrations observed in diabetic patients.Fig (5). In the present study,we found high levels of serum uric acid to be significant ( $P < 0.05$ ) in related to fasting serum glucose in diabetic patients Fig(3). Raised serum uric acid levels are commonly associated with high blood pressure<sup>(21)</sup> obesity<sup>(22)</sup> non insulin dependent diabetes mellitus<sup>(23)</sup> and glucose intolerance<sup>(24)</sup> Hyper-insulinemia are often associated with hyper uricemia or hyper tension<sup>(23, 25)</sup>. Insulin is related to serum uric acid level<sup>(25)</sup> and also increased sodium reabsorption through a direct action on the proximal tubule<sup>(26,27)</sup> One limitation of this study was our measurme of vit C concentration was based on a single serum vit C which indicate only the short term (1 to 4 weak) vitamin status of an individual<sup>(28)</sup>. We note that non of the studies examined urinary frequency, a factor we thought to be inveresly associated with serum vit C, Additoinally serum concentration of other antioxidants were not measured in this study, Thus ,we not be sure that the observed associations were due entirely to (vit C ,albumin, uric acid).Also we did not measure insulin level in our patient and our explanation remains there for speculative.



## Conclusion

Antioxidants like ( vit C ,albumin,uric acid ) may be beneficial as a possible markers for the identification of patients at risk from diseases such as diabetes mellitus or any inflammatory disease with oxidative damage.

## References

- 1-Halliwell, B. How to characterize a biological antioxidant. *Free. Radic. Res. Commun.* 1990;9:1 – 32.
- 2-“ Free Radicals Antioxidants , Aging and Disease” Knight, J.A. Ed, 1<sup>st</sup> edition, American association for clinical chemistry. 1999.
- 3-Martin, D. Free radical and antioxidants; clinical aspects. *Euroned.* 1997.
- 4- Dosoo, D.K. ; Rana, S.V. ;Maddy ,S.Q. ; et al . Total antioxidant status in type 2 diabetic patients in Ghana *Diabetes international* 2000 , 10 :26 – 27
- 5-Varley, H.; Gowenlock, A.H. and Bell , M. In” *Practical Clinical Biochemistry*” fifth ed., Vol. I, William Heinemann Medical Books LTD. London. 1980.
- 6-Doumas , B. T.; Watson, W.A. ;Biggs ,H.G. *Clin.Chim.Acta.* 1971; 31:87.
- 7- Barham and Trindar. *Analyst* . 1972;97:142.
- 8- Randox laboratories Ltd, Antrum , B1 29 4QY, UK. *Manual Procedures* , 4<sup>th</sup> edition 1996;126- 89.
- 9- Collier, A . ;Wilson, R.; Bradley, H. ;et al . Free radical activity in type 2 diabetes . *Diabetic Med* 1990; 7 : 27 – 30.
- 10- Lyons, T.J .Oxidized low-density lipoproteins :a role in the pathogenesis of atherosclerosis in diabetes. *Diabetic Med* 1991;8:411-19. 14
- 11- Wolf, S.P.; Dean, R.T. Glucose auto-oxidation and protein modification . The potential role of “autooxidative glycosylation” in diabetes. *Biochem J* 1987;245:243-50.
- 12- carriello ,A. ;Quatraro, A . ;Giugliano, D. New insights on non-enzymatic glycosylation may lead to therapeutic approaches for the prevention of diabetic complication. *Diabetic Med* 1992;9:297-9.
- 13-Will, J.C.; Byers, T. Does diabetes mellitus increase the requirements for vitamin C ? *Nur. Rev.* 1996;54:193 – 202.
- 14- Rimersa, R.A.; Wood, D.A.; Macintyre, C.C.; et al . Risk of angina pectoris and plasma concentrations of vitamin A, C and E and carotene . *Lancet* 1991;337:1-5.
- 15-The diabetes control and complications Trial Research group . The effect of intensive treatment of diabetes on the development of long term complications of insulin-dependent diabetes mellitus . *N Eng J Med* 1993,329:977-86.
- 16-Gougan, R. ;Pencharz, P.B.; and Sigal, R. J. Effect of glycemic control on the kinetics of whole – body protein metabolism in obese subjects with non insulin – dependent diabetes mellitus during iso and hypogenergic feeding. *AmJ Clin. Nutr.* 1997;65:861-70.



- 17-Anderson, J. W. ; Geil ,P.B: Nutritional management of diabetes mellitus. In: Shils, M.L.;Shike,J.M.; eds modern nutrition in health and disease.Philadelphia: Lea & Febigar, 1994:1259 –86.
- 18-Sinagra , D.; Scarpitta , A.M. ; et al .Serum protein changes in diabetes mellitus. *Minerva Medica* .1997;88:75 –9.
- 19-Castaneda. C.; Bermudez,O. ;and Tucker,K.I.. protein nutritional status and function are associated with type 2 diabetes in Hispanic elders.*Am. J . Clin. Nutr.* 2000;72:89 – 95.
- 20-Reuben , D.B. ;Moor, A.A.; Damesyn, M. ; et al .Correlation of hypoalbuminemia in community dwelling older persons. *Am. J.Clin Nutr.* 1997;66 :38 – 45.
- 21-Brecke nridge A. Hypertension and hyperuricaemia. *Lancet* . 1966;1:15-18
- 22-Cannon, P.J.;Stason, W.B.;Demartini, F.E. Hyperuricemia in primary and renal hypertension. *N Engl . J med.*1951;34:1421 – 1431..
- 23- Gertler , M.M.;Garn, S.M.; and Levine, S.A.Serum uric acid in relation to age and physique in health and coronary heart disease. *Ann Intern. Med* 1951;34:1421-1431
- 24- Tuomilehto ,J.; Zimmet, P. ;Wolf, E. ; et al .plasma uric acid level and it's association with diabetes mellitus and some biological parameters in a biracial population of Fiji . *Am . j .Epidemiol* ,1995 ;127: 321-336
- 25- Modan .M. ;Halkin, H.; Karasik ,A.; Lusky ,A. Elevated serum uric acid:a facet of hyperinsulinemia diabetologia.1987;30:713-718.
- 26- Ferrannini, E. ;Buzzigol , G .Bonadonna, R. ; et al . Insulin resistance in essential hypertension *N. Engl. J. Med* . 1987 , 317 : 350 – 357 .
- 27 – Defronzo ,R . The effect of insulin on renal sodium metabolism : a review with clinical implications . *Diabetologia* . ; 21 : 165–171.
- 28-Atherton , J.C. Green;R.; et al. Lithium clearance in man :effects of dietary salt intake ,acute changes in extra cellular fluid volume, amiloride and frusemide .*Clin . Sci.* 1987;72:201 – 208.