

Lipid Peroxidation and Antioxidant Status in Patients of End Stage Renal Disease with and without Pulmonary Tuberculosis.

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Abstract: A state of oxidative stress has been reported in chronic kidney disease (CKD) as well as in patients with tuberculosis. The incidence of infection with mycobacterium tuberculosis is significantly higher in patients with end stage renal disease and in cases of renal transplant when compared to otherwise normal individuals (10-16 times higher), there is paucity of literature regarding antioxidants and lipid peroxidation (LPO) in CKD patients with tuberculosis (TB) (ie dual disease). We assessed the antioxidants and LPO status in CKD patients who are on dialysis, on conservative management, in patients with tuberculosis. A comparison of antioxidants and LPO status between the patients and control subjects were analyzed. The oxidative stress and antioxidant status were evaluated in 102 individuals 63 males and 39 females. These individuals were grouped as follows Group I healthy volunteer (n=16), group II CKD patients not on dialysis (n=27), Group III CKD patients on hemodialysis (n=21) which further analysed as Group IIIA (before dialysis) and as Group IIIB (after dialysis), Group IV pulmonary tuberculosis (n=27) and group V CKD with pulmonary TB(n=11) which further analysed as Group VA (before dialysis) and Group VB (after dialysis), plasma LPO was assayed as measure of malondialdehyde (MDA) and enzymatic antioxidants levels such as that of superoxide dismutase (SOD), catalase, Glutathione peroxides (GPX) activity in erythrocytes. Vitamin C and Vitamin E were assayed in plasma as a measure of non enzymatic antioxidants. Compared to healthy volunteer the MDA levels were increased significantly in all the patients groups and antioxidants enzymes such as SOD, catalase, GPX, Vitamin E levels in CKD patients groups were significantly higher when compared to healthy volunteers and in patients with TB, however the levels in Vitamin E were significantly lower in patients with TB when compared to healthy volunteers. Determination of LPO, Antioxidants status including Vitamin C and Vitamin E is useful to evaluate the oxidative stress in these patients. Hemodialysis procedure alter LPO and antioxidant level of SOD, catalase, GPX, Vitamin C and Vitamin E in CKD in the presence of TB (dual disease).

INTRODUCTION

Free radicals are highly reactive species characterized by an unpaired electron in their outer orbital. Oxidative stress, which occurs when there are excessive free radical production or low antioxidant levels, has been reported in chronic kidney disease patients^{1,2}. Free radicals reactions including lipid peroxidation are considered to be important factors in pathogenesis of a variety of disease. These free radicals can damage proteins, lipids, carbohydrates and nucleic acids. Plasma membranes are critical target of free radical reactions. Oxygen derived free radicals can easily produce injuries to cell membranes by initiation of polyunsaturated fatty acid peroxidation, inactivation of membrane enzymes and receptors and protein cross linking fragmentation^{3,4}. Oxidative stress has been proposed to play a role in many states often associated with end stage renal disease, including cardiovascular, infectious disease, cancer, diabetes, disorders of peripheral and central nervous system, anemia and accelerated aging^{5,6,7}. Reactive oxygen species can attack any biochemical component of a cell and are postulated to be important mediators in the pathogenesis of experimental and clinical nephritis. In relation to high production of free radicals the risk of disease is high and current treatments to counteract uremia do not decrease the risk in these patients⁸. Mycobacterium can induce reactive oxygen species production by activating phagocytes⁹. In patients with pulmonary tuberculosis it has been reported that there is an increase in several circulating markers of free radical activity, some of which remains elevated even after completion of antimicrobial chemotherapy, indicating ongoing oxidative stress, which may contribute to the development of lung function abnormalities¹⁰.

It is difficult to quantitate free radicals because of their short half live and reactive nature. Therefore indirect methods measuring products of lipid peroxidation (as a measure by malondialdehyde concentration) and antioxidant enzymes like superoxide dismutase, catalase, glutathione peroxides and non enzymatic chain breaking antioxidants like Vitamin C, Vitamin E and A and carotenoids are preferred.

The study of red blood cells oxidative metabolism in chronic kidney disease (CKD) patients as well as CKD with pulmonary tuberculosis (dual disease) has been of interest and the results have not been very concordant. Thus the

aim of our study is to assess any changes in the antioxidant status and LPO in CKD, tuberculosis as well as in dual disease condition (ie CKD with TB).

MATERIALS AND METHODS

A total of 102 subjects of either sex were included based on urea, creatinine and creatinine clearance 9by applying Cockcroft and Gault formula), they were decided into five groups of whom 16 were healthy volunteers (Group I) with the mean age of 28±5 years (M-9; F-7); 27 were CKD patients not on dialysis (Group II) with the mean age of 35± 12 years (9M-20; F-7); 27 were CKD patients on regular hemodialysis (Group III) with the mean age of 35 ± 11 years (M-12; F-9) and they were subdivided in to two groups namely pre dialysis (Group IIIA) and post hemodialysis (Group IIIB); 27 were pulmonary tuberculosis (Group IV) with the mean age of 43 ± 8 years (M-16; F-11) and 11 were CKD/ Pulmonary tuberculosis on hemodialysis with the mean age of 45 ± 11 years (M-6; F-5) and they were subdivided in to two groups namely pre dialysis (Group VA) and post dialysis (Group VB). Patients with tuberculosis were included in the study in group IV and group V when the criteria of a positive chest X ray finding and a positive sputum acid fat bacilli (AFB) was met. Patients with diabetes, HIV and those on antioxidant supplementation were excluded from the study. The dialysis membrane used was Fresenius polysulfone membrane using acetate buffer. Duration of hemodialysis was 4 hours with the average speed of 200 ml/minute. After obtaining informed consent they were included in this study. Institutional Ethics Committee approved the study protocol.

COLLECTION OF BLOOD SAMPLING

Venous blood samples were collected in vacutainer tubes containing EDTA as an anticoagulant for all the patients. For patients who were undergoing hemodialysis, blood samples were collected prior to dialysis and at the end of dialysis.

PREPARATION OF HEMOLYSATE

The EDTA samples were centrifuged at 3000 rpm for 15 minutes to separate cells. Plasma was separated and the cells were resuspended with ice cold saline (0.9%) and washed with three time to obtain erythrocytes free from

other cells and plasma proteins. The parameters included plasma malondialdehyde (MDA) as a measure of lipid peroxidation (10), enzymatic antioxidants such as super oxide dismutase (SOD)¹¹, Catalase¹², Glutathione peroxidase (GPX)¹³ from erythrocytes (hemolysate) and non enzymatic antioxidants such as Vitamin-C¹⁴, and Vitamin-E¹⁵ from plasma. Hemoglobin concentration of hemolysate was determined by the method of Drabkin and Austin (1932) using cynomethemoglobin reagent. The value was expressed in g/dl.

STATISTICAL ANALYSIS

Differences among the groups were determined using an analysis of variance model (ANOVA). Multiple range tests by Tukey-HSD procedure was employed to identify the significance at 5% level. Student paired test t-test was also performed. A p-value less than 0.05 were considered as significant.

RESULTS

As shown in Table-1, when compared between the groups, the MDA levels were significantly increased in Group II, IIIA, IV and V A patients than the control subjects i.e. Group I (p<0.05). When CKD with TB group of V A was compared to the CKD groups there was a significant increased levels of MDA noted (p<0.05). The MDA levels of Group IV tuberculosis group compared with CKD groups of II, IIIA, VA the MDA levels were significantly increased (p<0.05). Plasma Vitamin E levels were significantly increased in groups of II, IIIA, VA when compared to Group I and Group IV (p<0.05), where as Vitamin E levels were significantly low in patients with tuberculosis (Group IV) when compared the control group (Group I). Erythrocytes SOD, GPX, Catalase activities and plasma Vitamin C levels were low in patients groups as compared to healthy volunteers (p<0.05).

As shown in Table-2, on comprising patients groups to healthy volunteers, MDA levels were significantly increased (p<0.05), whereas Group III B and Group V B of post dialysis (after dialysis) groups when compared to Group II of CKD with conservative management and Group IV (TB) the levels of MDA did not show any significant reduction (p>0.05). When CKD (Group II) is compared to the other groups the enzymatic antioxidants SOD, Catalase, GPX activities were increased (p<0.05); this shows that under conservative management there was an increased production of free radical damage. The mean values of patients in the dialysis groups were lower for Vitamin C and Vitamin E concentration when compared to the mean values of groups of subjects not on dialysis.

In Table-3 CKD of Group III A and group III B as well as CKD/ TB of Group VA and VB were compared before and after dialysis within the group respectively. After dialysis the MDA, Vitamin C and Vitamin E were significantly lowered when compared to the before dialysis groups. The antioxidants enzymes such as SOD, catalase, GPX were significantly increased after dialysis (p<0.05).

Table-1: Comparative Analysis of Antioxidant Status Between Groups

Parameter	Group I N=16	Group II N=27	Group III A N=21	Group IV N=27	Group V A N=11	Significant Groups at 5% level
SOD (units/gHb)	556.52 ± 36.59	411 ± 29.58	405.04 ± 11.64	464.22 ± 7.75	417.13 ± 13.20	I Vs II, IIIA, IV, VA IV Vs II, IIIA, VA
Catalase (μmoles of utilized/min)	1.88 ± 0.16	0.90 ± 0.06	0.90 ± 0.03	0.96 ± 0.02	0.89 ± 0.01	I Vs II, IIIA, V, VA IV Vs II, IIIA, VA
GPX (μmoles of GSH utilized/min/gHb)	48.10 ± 2.43	32.49 ± 2.58	31.02 ± 1.51	39.27 ± 0.62	32.11 ± 1.08	I Vs II, IIIA, IV, VA IV Vs II, IIIA, VA
Vitamin - C (mg/dl)	0.56 ± 0.03	0.36 ± 0.04	0.36 ± 0.02	0.41 ± 0.02	0.38 ± 0.01	I Vs II, IIIA, IV, VA IV Vs II, IIIA, VA
Vitamin-E (μg/ml)	10.69 ± 0.43	11.88 ± 0.13	11.78 ± 0.10	9.63 ± 0.32	11.86 ± 0.07	I, IV Vs II, IIIA, VA I Vs IV

The values are expressed as Mean ± SD. P<0.05 considered as significant Group I-Healthy volunteers, Group II-CKD patients not on dialysis, Group IIIA-CKD Patients pre-dialysis, Group-IV-Pulmonary Tuberculosis, Group VA-CKD/TB pre dialysis

Table-2: Comparative Analysis of Antioxidant Status Between groups

Parameter	Group I N=16	Group II N=27	Group III B N=21	Group IV N=27	Group V B N=11	Significant Groups at 5% level
SOD (units/gHb)	556.52 ± 36.59	411 ± 29.58	447.59 ± 7.21	464.22 ± 7.75	446.22 ± 6.07	I Vs II, IIIB, IV, VB II Vs IIIB, IV, VB
Catalase (μmoles of H ₂ O ₂ utilized/min)	1.88 ± 0.16	0.90 ± 0.06	1.01 ± 0.07	0.96 ± 0.02	1.00 ± 0.01	I Vs, II, IIIB, IV, VB II Vs IIIB, IV, VB
GPX (μmoles of GSH utilized/min/gHb)	48.10 ± 2.43	32.49 ± 2.58	37.99 ± 1.71	39.27 ± 0.62	37.03 ± 1.08	I Vs II, IIIB, IV, VB II Vs, IIIB, VB
Vitamin - C (mg/dl)	0.56 ± 0.03	0.36 ± 0.04	0.36 ± 0.02	0.41 ± 0.02	0.32 ± 0.01	I Vs II, IIIB, IV, Vs II, IIIB, VB II Vs IIIB, VB
Vitamin-E (μg/ml)	10.69 ± 0.43	11.88 ± 0.13	11.67 ± 0.09	9.63 ± 0.32	11.77 ± 0.06	I, IV Vs IIIB, VB I Vs IV

The values are expressed as Mean ± SD. P<0.05 considered as significant Group I-Healthy volunteers, Group II-CKD patients not on dialysis, Group III B**- CKD patients post-dialysis, group IV-Pulmonary Tuberculosis, Group VB**-CKD/TB post dialysis

Table-3: Paired samples of Chronic kidney disease and CKD/TB (pre and post dialysis)

Parameters	Group III A N=21	Group III B N=21	Change	Group V A N=11	Group V B N=11	Change
SOD (units/gHb)	405.04 ± 11.64	447.59 ± 7.21	42.55* ± 9.10	417.134 ± 13.20	446.78 ± 6.07	29.65* ± 9.22
Catalase (μmoles of H ₂ O ₂ utilized/min)	0.90 ± 0.03	29.65 ± 9.22	0.11* ± 0.05	0.89 ± 0.01	1.00 ± 0.04	0.11* ± 0.03
GPX (μmoles of GSH utilized/min/gHb)	31.02 ± 1.51	31.02 ± 0.03	6.97* ± 0.63	32.11 ± 1.08	37.03 ± 1.08	4.92* ± 0.46
Vitamin - C (mg/dl)	0.36 ± 0.02	4.92 ± 0.46	-0.05* ± 0.01	0.38 ± 0.01	0.32 ± 0.01	-0.06* ± 0.01
Vitamin-E (μg/ml)	11.78 ± 0.10	-0.06 ± 0.01	-0.11* ± 0.06	11.86 ± 0.07	11.77 ± 0.07	-0.09* ± 0.02

T*Student's paired t-test was used to calculate the p Value. * p value <0.05 considered as significant. The values are expressed as Mean ± SD Group IIIA-CKD patients pre-dialysis, group III B-CKD patients post-dialysis Group V A-CKD/TB patients pre-dialysis, group V B-CKD/TB patients post-dialysis

Table-4: Biochemical parameters compared between the Groups

Parameter	Group I N=16	Group II N=27	Group III A N=21	Group IV N=27	Group V A N=11	p-Value*	Significant# Groups at 5% level
Hb g/dl	12.39 ± 0.99	7.33 ± 1.38	6.85 ± 0.99	7.84 ± 1.14	7.01 ± 0.94	<0.001	I vs II, III, IV, V, Vs III vs IV
Urea Mg/dl	22.6 ± 2.2	133 ± 18.6	108.7 ± 25.2	21.6 ± 4.8	128.5 ± 4.8	<0.001 (S)	II, III, V, Vs I, IV
Creatinine Mg/dl	0.76 ± 0.08	9.69 ± 1.47	6.05 ± 1.67	0.79 ± 0.11	7.89 ± 1.64	<0.001 (S)	I, III, V Vs I, IV
Uric acid Mg/dl	4.2 ± 0.7	8.1 ± 1.2	8.1 ± 1.0	4.0 ± 1.1	7.8 ± 0.9	<0.001 (S)	II, III, V Vs I, IV
Creatinine clearance	125.7 ± 28.0	8.4 ± 2.1	13.9 ± 3.8	110.5 ± 12.2	8.7 ± 3.0	<0.001 (S)	II, III, V Vs I, IV
Bilirubin Mg/dl	0.7 ± 0.2	0.8 ± 0.1	0.7 ± 0.1	0.7 ± 0.2	0.6 ± 0.1	0.10 (NS)	NIL
Total Protein Mg/dl	7.0 ± 0.4	5.2 ± 0.4	5.6 ± 0.2	6.1 ± 0.3	5.9 ± 0.3	<0.001 (S)	I vs II, III, IV, V IV Vs II, III, III, V Vs II
BUN Mg/dl	10.57 ± 1.04	61.8 ± 9.06	50.76 ± 1.78	10.06 ± 2.24	59.77 ± 7.58	<0.001 (S)	II, III, V Vs I, IV

The values are expressed as Mean ± SD

*One-way ANOVA was used to calculate the p-value. # Multiple range test by Turkey-HSD procedure was employed to identify the significant at 5% level

DISCUSSION

In the present study there was a significant lower mean levels of antioxidant enzymes as observed by the levels of SOD, catalase, GPX in group II, Group IIIA, group IV and Group VA when compared to healthy volunteers of group I. the cell damage within the erythrocytes caused by free radical is avoided by copper-Zinc superoxide dismutase enzyme. This enzyme catalyses dismutation of superoxide radical in to molecular oxygen and hydrogen peroxide. The inhibition of SOD leads to reduction in the survival of cells. Because of the decreased GPX activity in erythrocytes the accumulation of

hydrogen peroxide may cause inhibition of SOD activity¹⁶. On comparison between pre and post dialysis groups the antioxidant enzymes levels of SOD, catalases, GPX were significantly increased. There is conflicting report on the antioxidant level during dialysis; some authors have registered no change¹⁷, whereas some have reported decreased levels and some have reported increased levels^{18,19}. Our study shows increase of antioxidant level during dialysis. When Group II, IIIA and Group VA were compared with group IV of tuberculosis group it was found that the levels of antioxidant enzymes such as SOD, catalase, GPX were significantly lower. This shows that in patients renal disease with and tuberculosis (dual disease), the antioxidant enzymes are further diminished when compared to patients who had pulmonary tuberculosis alone. The levels of vitamin C were significantly lower in group II, IIIA, IV and VA when compared to Group I. During dialysis Vitamin C was significantly reduced indicating that it is lost in the dialysate as it is water soluble. It has been suggested that concentration of Vitamin C in hemodialyzed patients are lower than those of controls, and they fall even further after hemodialysis²⁰. This further supports the study that there is depletion of vitamin C in CKD patients. When CKD patients of Group II, III and V compared to patients with pulmonary tuberculosis (Group IV), vitamin C levels were significantly low in CKD groups. In order to restrict potassium intake, most dialysis patients are advised to consume only a very limited amount of fruits, the dietary intake of vitamin C, is likely to be poor. Non enzymatic antioxidant of Vitamin E was significantly reduced. Plasma Vitamin E levels are reported to be highly variable in CKD and patients on hemodialysis but not routinely depressed and may even be elevated above control levels²¹. High plasma Vitamin E levels were observed in patients with CKD²². According to Syein G et al²³ reported that under normal conditions of conservative or dialysis treatment of CKD patients, Vitamin E seems not to be a factor concerning uremic symptoms and there seems to be no need for Vitamin E supplementation. This further supports this studies observation. However in patients with tuberculosis Vitamin E levels were low when compared to controls. Ongoing activation of lung macrophage and associated free radical mediated pulmonary fibrosis may result in chronic oxidative stress with consequent diversion of Vitamin E to the lungs of patients with pulmonary underlying the increase of Vitamin E is not clear. Lipid peroxidation as a measured by levels of MDA was significantly increased in Group II, III, IV and V when compared to group I of healthy subjects. When the mean of pre and post dialysis levels of MDA are compared the level of MDA was lower in post hemodialysis. This shows that during the MDA levels reduced due to the removal of uremic toxins, corrections of azotemia and improvement in cardiovascular status after dialysis^{24, 25, 26}. The levels of MDA in patients with tuberculosis were significantly lower than that of CKD patients. This shows that CKD patients have more antioxidant stress than that of tuberculosis patients. In CKD / TB patients the MDA levels were significantly increased that that of Group II, Group IV. This show that in dual disease there is ongoing high level of oxidant stress observed.

CONCLUSIONS

Evaluation of plasma malondialdehyde (MDA) as a measure of lipid peroxidation and estimation of antioxidant enzymes can lead to a better understanding of free radical damage as a result of oxidative stress in patients of CKD, patients with pulmonary tuberculosis and those of CKD with TB. In patients with CKD and in those with pulmonary tuberculosis, the mean plasma MDA levels were higher and the hemolysate concentrations of antioxidants enzymes were lower than in healthy volunteers. The mean levels of these substances were slightly lower in patients with pulmonary tuberculosis when compared to that of the levels in patients with CKD.

However, Vitamin E levels were found to be greater in patients with CKD when compared to healthy volunteers and in patients with tuberculosis. The mechanism behind the increased levels of Vitamin E in patients with CKD would need further study. In patients with CKD and tuberculosis, the mean plasma MDA levels were found to be higher and levels of antioxidant enzymes were lower than the healthy volunteers. When comparing the mean values of MDA in patients with CKD, tuberculosis and patients of CKD with pulmonary tuberculosis it was found that the mean levels of MDA was significantly higher in the patients with CKD and Tuberculosis. The increased MDA levels and lower antioxidant enzymes levels in patients with CKD and tuberculosis denotes the increased free radical damage in these patients when compared to patients with either of these conditions separately.

REFERENCES

1. **Descamps-Latcha B.** Phagocyte oxidative metabolism in hemodialysis. *Contrib Nephrol.* 1998; 62:32-39.
2. **Loughrey CM., Yung IS., Light Body JH., Mc Master D., Mc Namee PT., Trimble ER.** Oxidative stress in hemodialysis. *QJ Med.* 1994; 87:679-683.
3. **Yamata Y., How R., Jacob H.** Abnormal red cell metabolism causing hemolysis in Uremia. *Ann Int Med.* 1974; 78:360-362.
4. **Chauhan DP, Gupta PH, Namporthic MRN, Singal PC.** Determination of RBC Superoxide dismutase, catalase, reduced glutathione and MDA in uremia. *Clinica Chem. Acta.* 1982; 123:153-159.
5. **Hasselwander O, Young IS.** Oxidative stress in chronic renal failure. *Free radical Res.* 1998; 29:1-11.
6. **Galli F., Canevari F., Bellomo G.** Physiopathology of the oxidative stress and its complications in uremia and dialysis. In: Ronco C, La Greca G (eds) *Vitamin E bonded membrane. A further step in dialysis optimization.* *Contrib Nephrol.* 1999; 127:1-31.
7. **Tetta C., Biasioli S., Schiavon R., Inguaggiato P., David S., Panichi V., Wratten ML.** An overview of hemodialysis and oxidative stress. *Blood purif.* 1999;17:118-126.
8. **Hartika Yamada, Yasukazu Yamada, Testuo Adachi, Atsushi Fukatsu, Masato sakuma, AroFutenma, Shinichi kakuma.** Protective role of extracellular superoxide dismutase in hemodialysis patients. *Nephron.* 2000;84:218-223.
9. **May ME., Spagnuolo PJ.** Evidence for activation of a respiratory burst in the interaction of human neutrophils with *Mycobacterium Tuberculosis.* *Infect immune.* 1985;55:2304-2307.
10. **Jack CIA., Jackson MJ., Hind CRK.** Circulating markers of free radicals activity in patients with pulmonary tuberculosis. *Tubercle Lung Dis.* 1994;75:132-137.
11. **Markuland G., Markuland S.** Involvement of the superoxide anion radical in the autooxidation of pyrogallol and a convenient assay of super oxide dismutase. *Eur. J. Biochem* 1974;47:469-474.
12. **Sinha AK.** Colorimetric assay of catalase. *Anal. Biochem.* 1972;47:389-394.
13. **Rotruck JT., Pope AL., Ganther HE., Swanson AB., Hafeman DG, Hoekstra WG.** Selenium: Biochemical role as a component of glutathione peroxidase. *Science.* 1973; 179:588-590.
14. **Omay ST., Trunbull JD., Sauberlich HE.** Selected methods for the determination of ascorbic acid in animal cells, tissues and fluids. *Method Enzymol.* 1971;62:1-11.
15. **Desai ID.** Vitamin E analysis method for animal tissues. *Methods Enzymol.* 1984;105:138-144.
16. **Bast A., Haenen GRMM., Doelman CJA.** Oxidants and antioxidants; state of the art. *Am J med.* 1991;91 (suppl. 3c):25-135.
17. **Lin TH., Chen JG., Laiw JM., Jaung JG.** Trace elements and lipid peroxidation in Uremic patients on hemodialysis. *Biol Trace Elem. Res.* 1996;5:277-283.
18. **Ayemek Gonenc., Yesin Atak., Mehmet Nroman., Bolkan Sunsek.** Lipid peroxidation and antioxidant systems in hemodialyzed patients. *Nephrol Dial Transplantation.* 2002;33(2):11-15.
19. **Toberk M., wasik T., Drozd M., Klin M., Magner Woobel K., HKopieczna-Grzebeniak E.** Effect of hemodialysis on lipid peroxidation and antioxidant system in patients with chronic renal failure. *Metabolism.* 1992;41:1229-1232.
20. **Clermont G., Lecours., Lahet JJ., etal.** Alteration in plasma antioxidants capacities in chronic renal failure and hemodialysis patients; A possible explanation for the increased cardio vascular risk in these patients. *Cardiovasc Rs.* 2000;47:618-623.
21. **Bonnefont-Rousselet D., Jaudon MC., Issad B., Cacoub P., Congy F., Jardel C., Delatre J., Jacobs C.** Antioxidants status of elderly chronic renal patients treated by continuous ambulatory peritoneal dialysis. *Nephrol Dial Transplant.* 1997; 12:1399-1405.
22. **Girelli D., Lupo A., Trevisan MT., Olivieri O., Bernich P., Bassi A., Stanzial AM., Ferrari S., Corrocher R.** Red blood cell susceptibility to lipid peroxidation, membrane lipid composition and antioxidant enzymes in continuous ambulatory peritoneal dialysis patients. *Perit Dial Int.* 1992; 12:205-210.
23. **Stein G., Richter G., Funstuck R., Sperschneider H., Gunther K.** Serum vitamin E levels in patients with chronic renal failure. *Int J. Artif organs.* 1983;6(6): 285-287.
24. **Yalcin As., Yurtkuran M., Dilek M., Kilinc A., Taha Y., Emerk K.** The effect of vitamin E therapy on plasma and erythrocyte lipid peroxidation in chronic hemodialysis patients. *Clin Chem Acta.* 1989; 185:109-112.
25. **Taccone- Galucci M., Giardini O., Lubrano R., bandino D., Casciani CU.** Red blood cell lipid peroxidation in predialysis chronic renal failure. *Clin Nephrol.* 1992; 38:48-55.
26. **Goncagul H., Yeganaga I., Suha AY.** Evaluation of oxidant stress in chronic hemodialysis patients, use of different parameters. *Clinica Chem Acta.* 1995;239:109-114.

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