Original Article

# Evaluation of oxidative stress and thyroid hormone status in hemodialysis patients in Gorgan

**Javad Velayeti, Azad Reza Mansourian[1], Mohammad Mojerloo[2], Abdoljalal Marjani[1]**

*Student Research Committee, [1]Metabolic Disorders Research Center, Departments of Biochemistry and Biophysics and [2]Internal Medicine, Gorgan Faculty of Medicine, Golestan University of Medical Sciences, Gorgan, Golestan Province, Iran*

## ABSTRACT

**Aims:** The aim of this study focused on serum malondialdehyde (MDA) levels and erythrocyte superoxide dismutase (SOD) and catalase (CAT) activities in hemodialysis patients and compared with control groups. **Materials and Methods:** Forty-five hemodialyzed patients and 45 control groups recruited in this study. Serum creatinine and urea, thyroid hormones (THs) levels and erythrocyte antioxidant enzyme activities were determined. **Results:** Hemodialysis (HD) patients showed higher levels of MDA than control groups ($P < 0.01$), but the levels of thyroxin (T3), free triiodothyronine (fT3), and free thyroxin (fT4), SOD and CAT were low in HD patients ($P < 0.01$). Serum T3, fT3, and fT4 levels were significantly negative correlated with MDA ($P < 0.01$). **Conclusion:** It is concluded that serum lipid peroxidation is markedly increased in HD patients. This means that elevated reactive oxygen species may interact with the lipid molecules in HD patients. HD may cause significant changes in TH levels. Thyroid-stimulating hormone level in HD patients is slightly similar to that of control groups. This suggests that thyroid is able to resynthesize for hormonal urinary losses.

**Key words:** Antioxidant enzymes, hemodialysis, lipid peroxidation, thyroid hormones

## Introduction

Thyroid hormones (THs) are necessary for metabolic function of the kidneys. The kidney is an organ for metabolism and elimination of THs and a target of some of the iodothyronines' actions. Thyroid dysfunction may effect on glomerular and tubular functions and electrolyte and water ($H_2O$) homeostasis. It may cause a reduction in glomerular filtration, hyponatremia, and $H_2O$ excretion alteration.[1-3] Many studies have shown that patients on regular hemodialysis (HD) tolerate a chronic illness which was not involved the thyroid, but these patients indicated low serum thyroxin (T4) and triiodothyronine (T3) levels.[4,5] Some studies revealed decreased T3 and T4 levels while the thyroid-stimulating hormone (TSH) levels are not elevated.[6] There may be an association between THs and the oxidative and antioxidative status in the body. It has been reported that thyroid dysfunction such as hypothyroidism reduces oxidant production which may not protect the organism against oxidant damage.[7,8] There are limited and controversial studies on the oxidative status of hypothyroidism.[9-11] Different antioxidant enzymes may protect oxidative effects of free radicals on lipids, proteins, and DNA. These enzymes consist of superoxide dismutase (SOD) and catalase (CAT).[12] SOD catalyzes the alteration of the superoxide anion into hydrogen peroxide ($H_2O_2$). $H_2O_2$ then changed to $H_2O$ by CAT or glutathione peroxidase.[13,14] Lipid peroxidation which express as malondialdehyde (MDA) may change in different age and ethnic groups, gender and different kinds of diseases.[15-21] HD is the most effective method in balancing the metabolic

**Corresponding Author:** Dr. Abdoljalal Marjani, Department of Biochemistry and Biophysics, Metabolic Disorders Research Center, Gorgan Faculty of Medicine, Golestan University of Medical Sciences, Gorgan, Golestan Province, Iran. E-mail: abdoljalal@yahoo.com

| Access this article online | |
|---|---|
| Quick Response Code: | Website: www.ijem.in |
| | DOI: 10.4103/2230-8210.179986 |



**Cite this article as:** Velayeti J, Mansourian AR, Mojerloo M, Marjani A. Evaluation of oxidative stress and thyroid hormone status in hemodialysis patients in Gorgan. Indian J Endocr Metab 2016;20:348-53.

abnormalities related to renal oxidative stress that causes to morbidity in HD patients.[22] Chronic renal failure (CRF) patients who are on HD therapy show a high percentage of goiter and thyroid dysfunction and cardiovascular (CV) disorders.[23-25] Free radicals have been revealed to change the activity of some membrane-bound tissue enzymes.[26] End-stage renal disease can only be overcome by hemodialysis which can be considered as crucial therapeutic regiments for such kidney diseases and for those subjects which are a candidate for kidney transplantation.[27] The production of reactive oxygen species (ROS) which are the byproducts of hemodialysis therapy is the main obstacle and complications in hemodialysis application for the end stage renal failure.[28-30] THs can be altered due to hemodialysis. The THs abnormality may accompany with various disorders, including systemic acidosis, the hemodialysis duration, and endothelial injuries and inflammation.[31] The aim of this study focused on serum MDA levels which is an indicator of lipid peroxidation and erythrocyte SOD and CAT activities in hemodialysis patients and compared with age-matched control groups in Gorgan.

## Materials and Methods

Forty-five hemodialyzed patients with mean age 51.88 ± 15.90 years who were referred to the HD unit at 5th Azar Education Hospital of Gorgan Faculty of Medicine, Golestan University of Medical Sciences in Gorgan, Iran in 2015. Patients were compared with 45 age-matched control groups (mean age 48.68 ± 15.60). This study was approved by the Research Deputy Ethics Committee of the Golestan University of Medical Sciences. An informed consent from all subjects had been carried out. HD patients were being treated 3 times a week. Clinical history test was performed from all patients. Patients with diabetes mellitus, liver disease, endocrinal diseases, acute or chronic illness, thyroid disorders and any drug that affect TH were excluded from the study. A 10 ml blood samples were provided after an overnight fast of 12 h. Biochemical tests including serum creatinine and urea, THs (TSH, T3, T4, free triiodothyronine [fT3] and free thyroxin [fT4]) and erythrocyte antioxidant enzymes (SOD [Code number: 706002, Cayman Chemical Commercial Kit, Colorimetric Method, USA] and CAT [Code Number: 707002, Cayman Chemical Commercial Kit, Colorimetric Method, USA]) were determined. The hormonal analysis was done by Monobind Kit (Code Number: 1225-300, Lake Forest CA: 92630, USA) and enzyme immunoassay (ELISA) method. Serum creatinine and urea levels were determined with commercial kits by spectrophotometer techniques (Model JENWAY 6105 UV/VIS) in the Metabolic Disorders Research Center (Gorgan Faculty of Medicine). Serum MDA was determined with Kei Satoh method.[32] Weight was measured, while subjects were minimally clothed without shoes, using digital scales. Height was measured in standing position using tape meter while the shoulder was in a normal position. Body mass index (BMI) was defined as weight in kilograms divided by height in meters squared. Overweight was defined as BMI 25.0–29.9 kg/m$^2$ and obese as BMI ≥30 kg/m$^2$.[33]

The results are shown as means and standard deviations. SPSS version 16 (SPSS Inc., Chicago, IL, USA) software was used to calculate the statistical analysis. The evaluation of data was done by using independent sample *t*-test and Pearson correlation test. $P < 0.05$ was considered statistically significant.

## Results

Table 1 shows clinical and anthropometric characteristics of the HD patients and control groups. There was no difference in serum TSH, age, and BMI among the studied groups. There were well-significant differences in serum T3, T4, fT3 and fT4, MDA, SOD, and CAT compared with control groups. HD patients showed higher levels of MDA than those control groups ($P < 0.01$), but the levels of T3, fT3 and fT4, SOD and CAT were low in HD patients ($P < 0.01$). Table 2 shows relationship between MDA SOD and CAT and THs in HD patients. Spearman correlation analysis showed that the serum T3, fT3, and fT4 levels were significantly negative correlated with MDA [Table 2]. There was no correlation between THs and SOD and CAT.

## Discussion

In the present study, we revealed that the thyroid function differed among the HD group compared to the healthy

**Table 1: Clinical data of study subjects**

| Parameters | Healthy subjects | Hemodialysis patients | *P* |
|---|---|---|---|
| *n* | 45 | 45 | - |
| Age (years) | 48.68±15.6 | 51.88±15.9 | 0.330 |
| BMI (kg/m$^2$) | 26.41±2.81 | 25.92±6.67 | 0.653 |
| TSH (mIU/mL) | 2.13±0.84 | 2.76±2.21 | 0.079 |
| T3 (ng/mL) | 1.25±0.25 | 0.83±0.32 | 0.001 |
| T4 (μg/dL) | 7.97±1.17 | 7.53±2.12 | 0.222 |
| fT3 (pg/mL) | 2.78±0.43 | 2.51±0.59 | 0.013 |
| fT4 (ng/dL) | 1.35±0.18 | 0.92±0.31 | 0.001 |
| Creatinine (mg/dL) | 0.91±0.77 | 10.03±1.92 | 0.001 |
| Urea (mg/dL) | 24.72±2.65 | 103.86±25.9 | 0.001 |
| SOD (U/mL) | 0.15±0.04 | 0.08±0.13 | 0.002 |
| CAT (nmol/min/mL) | 16.43±7.04 | 12.31±6.80 | 0.001 |
| MDA (nmol/mL) | 0.45±1.14 | 2.98±0.89 | 0.001 |

BMI: Body mass index, TSH: Thyroid-stimulating hormone, fT3: Free triiodothyronine, fT4: Free thyroxin, SOD: Superoxide dismutase, CAT: Catalase, MDA: Malondialdehyde, T3: Triiodothyronine, T4: Thyroxin

**Table 2: Correlation analyses between oxidative stress biomarkers and thyroid hormones in hemodialysis subjects**

| Parameters | CAT | SOD | MDA |
|---|---|---|---|
| TSH | *r*=−0.016 | *r*=−0.071 | *r*=0.037 |
| | *P*=0.883 | *P*=0.506 | *P*=0.730 |
| T3 | *r*=0.153 | *r*=0.186 | *r*=−0.499* |
| | *P*=0.150 | *P*=0.08 | *P*=0.001 |
| fT3 | *r*=−0.145 | *r*=0.057 | *r*=−0.321* |
| | *P*=0.173 | *P*=0.593 | *P*=0.002 |
| T4 | *r*=−0.039 | *r*=−0.167 | *r*=−0.161 |
| | *P*=0.716 | *P*=0.125 | *P*=0.129 |
| fT4 | *r*=0.172 | *r*=0.239 | *r*=−0.521* |
| | *P*=0.104 | *P*=0.053 | *P*=0.001 |

*r= -0.499, *P*=0.001, SOD: Superoxide dismutase, CAT: Catalase, MDA: Malondialdehyde, TSH: Thyroid-stimulating hormone, T3: Triiodothyronine, T4: Thyroxin, fT3: Free triiodothyronine, fT4: Free thyroxin

controls. Serum T3, fT3, and fT4 levels were lower; TSH was slightly higher, and T4 was unchanged among those with HD. Serum lipid peroxidation and antioxidant enzyme activities were significantly high and low among the HD group compared to the healthy controls, respectively. Some studies have shown a low serum level of T3 in patients with end-stage renal disease (ESRD).[34-41] Lim *et al*.[35] reported a reduced T3 level and decreased conversion of T4 to T3 in uremic patients.[35] It is also revealed low serum T4 or fT4 levels in patients undergoing maintenance HD.[5,36,37,39,40] The serum TSH level in patients with CRF[34-37,41,42] had been reported to be almost normal. Our study showed that the serum TSH level in the HD patients slightly increased and serum fT3 and fT4 level significantly decreased which is in agreement with other studies.[5,39,40,43-51] In our study, slightly increase of TSH level in hemodialyzed patients in comparison to control groups was not in accordance with others studies.[52] The increase in the serum TSH level was not obvious in HD patients. The low serum fT4 and fT3 levels may be responsible for the low metabolism of the body. Studies on a uremic rat model have shown that there may be a difference in the TH metabolism or action in the peripheral system and in the central nervous system in the ESRD patients.[53,54] Xess *et al*. showed that CRF patients revealed a significant decrease in T3 (in accordance with our study) and T4 (not in accordance with our study) levels in comparison to control groups,[6,41,55] but serum TSH levels indicated no significant difference in patients and control groups which was in agreement with other findings.[55] The movement of TH into and out of the extravascular space may be a possible mechanism of TH changes related to HD.[6] There are different findings on variations in serum lipid peroxidation level and erythrocyte antioxidant enzyme activities due to HD. Some studies indicated an increase while some show a decrease in the levels. In our study, we determined the level of serum MDA of HD patients. MDA uses as a specific and sensitive biomarker for the estimation of the lipid peroxidation status in different diseases,[56] including in patients under chronic HD treatment.[57] Our results show a significant increase of serum MDA in the HD group when compared with the control group. Oxidative damage may depend on different risk factors, but it can be caused by the imbalance between the productions of free radicals and different anti-oxidant enzymes.[58] Lipid peroxidation disrupts the structural integrity of the lipid bilayer, leading to elevated membrane permeability (the release of hydrolytic enzymes and increasing cell damage) and subsequent impaired electron transport for oxidative phosphorylation in mitochondria and increased lysosomal permeability.[59] The results of present study indicate that significant difference of anti-oxidant enzyme activities between HD and control group may be related with the loss of antioxidant enzymes, and the reduction of antioxidant enzymes may be related to elevation of lipid peroxidation in hemodialyzed patients which is in agreement with findings of other studies.[58,60,61] These results show that oxidants and anti-oxidants imbalance may play an important role in the pathogenesis of some diseases. Some findings showed that the elevated MDA level may act as a metabolic signal for kidney damage and protein leakage including THs.[62] It is reported that there is a significant increase of the blood SOD and CAT activity in plasma and red blood cells of patients undergoing hemodialysis.[61] Some other studies also indicated that the activity of erythrocyte SOD and CAT increased significantly[63,64] while another finding showed a decrease of antioxidant enzymes in erythrocyte of CRF patients.[65-69] Study on hemodialyzed patients showed that significantly lower plasma CAT activity was found.[65] Study on the animal model kidney of the cytoplasmic SOD has revealed the decrease of the SOD protein abundance in the kidney tissues of the CRF animals which is in accordance with findings that reported the decrease of SOD enzymatic activity in the erythrocytes of patients with CRF[70-72] and in our results. We found significantly positive correlation between T3, fT3, and fT4 and MDA, which is not in agreement with other studies.[42] This correlation between MDA and above mentioned TH levels indicate that the alteration of these hormone levels in hemodialyzed patients may depend on variations of lipid peroxidation in these patients. Reduced serum fT3 and T3 may also relate to impaired extrathyroidal changing of T4 to T3. The alteration of T4 and fT4 are less considered in these patients.[73] The exact mechanisms for the decrease of T3 are not well known, but some studies have shown that the decreased T3 level correlates with poor cardiac prognosis and a strong predictor of death in cardiac patients.[74] Decreased fT3 is not only important in CRF patients but also in acute and chronic infections; diabetes; and different CV diseases.[74] Studies have shown that T3 and fT3 are as survival markers in patients with CKD and in

HD patients.[75] Some researchers have suggested that there is a relationship between T3 levels and thyroid dysfunction and risk of mortality in these patients.[76]

## Conclusion

Thyroid dysfunction in HD patients is more common than in general population. HD may influences thyroid function in various ways. Serum lipid peroxidation is markedly increased in HD patients. This means that elevated ROS may interact with the lipid molecules in HD patients. Our results suggest that HD may cause significant changes in TH levels. TSH level in HD patients is slightly similar to that of control groups. This suggests that thyroid is able to re-synthesize for hormonal urinary losses. Because of the high prevalence of thyroid dysfunction in HD patients, it suggests that screening of thyroid function should be needed.

### Financial support and sponsorship

Nil.

### Conflicts of interest

There are no conflicts of interest.

## References

1. Kelly GS. Peripheral metabolism of thyroid hormones: A review. Altern Med Rev 2000;5:306-33.
2. Ichikawa I, Kiyama S, Yoshioka T. Renal antioxidant enzymes: Their regulation and function. Kidney Int 1994;45:1-9.
3. Stratta P, Canavese C, Dogliani M, Mazzucco G, Monga G, Vercellone A. The role of free radicals in the progression of renal disease. Am J Kidney Dis 1991;17 5 Suppl 1:33-7.
4. Van Leusen R, Meinders AE. Cyclical changes in serum thyroid hormone concentrations related to hemodialysis: Movement of hormone into and out of the extravascular space as a possible mechanism. Clin Nephrol 1982;18:193-9.
5. Sakurai S, Hara Y, Miura S, Urabe M, Inoue K, Tanikawa T, *et al.* Thyroid functions before and after maintenance hemodialysis in patients with chronic renal failure. Endocrinol Jpn 1988;35:865-76.
6. Alsaran K, Sabry A, Alshahhat H, Babgy E, Alzahrani F. Free thyroxine, free triiodothyronine and thyroid-stimulating hormone before and after hemodialysis in Saudi patients with end-stage renal disease: Is there any difference? Saudi J Kidney Dis Transpl 2011;22:917-21.
7. Coria MJ, Pastrán AI, Gimenez MS. Serum oxidative stress parameters of women with hypothyroidism. Acta Biomed 2009;80:135-9.
8. Messarah M, Boumendjel A, Chouabia A, Klibet F, Abdennour C, Boulakoud MS, *et al.* Influence of thyroid dysfunction on liver lipid peroxidation and antioxidant status in experimental rats. Exp Toxicol Pathol 2010;62:301-10.
9. Dumitriu L, Bartoc R, Ursu H, Purice M, Ionescu V. Significance of high levels of serum malonyl dialdehyde (MDA) and ceruloplasmin (CP) in hyper-and hypothyroidism. Endocrinologie 1988;26:35-8.
10. Konukoglu D, Ercan M, Hatemi H. Plasma viscosity in female patients with hypothyroidism: Effects of oxidative stress and cholesterol. Clin Hemorheol Microcirc 2002;27:107-13.
11. Torun AN, Kulaksizoglu S, Kulaksizoglu M, Pamuk BO, Isbilen E, Tutuncu NB. Serum total antioxidant status and lipid peroxidation marker malondialdehyde levels in overt and subclinical hypothyroidism. Clin Endocrinol (Oxf) 2009;70:469-74.
12. Serdar Z, Aslan K, Dirican M, Sarandöl E, Yesilbursa D, Serdar A. Lipid and protein oxidation and antioxidant status in patients with angiographically proven coronary artery disease. Clin Biochem 2006;39:794-803.
13. Das K, Chainy GB. Thyroid hormone influences antioxidant defense system in adult rat brain. Neurochem Res 2004;29:1755-66.
14. Senthil S, Veerappan RM, Ramakrishna Rao M, Pugalendi KV. Oxidative stress and antioxidants in patients with cardiogenic shock complicating acute myocardial infarction. Clin Chim Acta 2004;348:131-7.
15. Marjani A. Lipid peroxidation alterations in type 2 diabetic patients. Pak J Biol Sci 2010;13:723-30.
16. Marjani A, Veghari G, Badeleh MT. Serum lipidperoxidation and leptin levels in male and female type 2 diabetic patients in Gorgan (South East of Caspian Sea), Iran. J Chin Clin Med 2010;5:26-35.
17. Marjani A, Mansourian AR, Ghaemi EO, Ahmadi A, Khori V. Lipid peroxidation in the serum of hypothyroid patients (In Gorgan-South East of Caspian Sea). Asian J Cell Biol 2008;3:47-50.
18. Marjani A, Mansourian AR, Veghari GR, Rabiee MR. Age-related alterations of plasma lipid peroxidation and erythrocyte superoxide dismutase activity in different ethnic groups of Gorgan. J Appl Sci 2007;7:1795-9.
19. Marjani A, Moradi A, Saeedi M. Plasma lipid peroxidation zinc and erythrocyte Cu-Zn superoxide dismutase enzyme activity in patients with type 2 diabetes mellitus in Gorgan city (South East of the Caspian Sea). J Med Sci 2007;7:585-90.
20. Marjani A. Effect of haemodialysis on plasma lipid peroxidation and endogenous non-enzymic antioxidants in Gorgan (South East of Caspian Sea). J Med Sci 2006;6:681-5.
21. Marjani A. Age-related alterations of plasma lipid peroxidation and erythrocyte superoxide dismutase activity in different age groups of Gorgan City, Iran. Saudi Med J 2005;26:1647-8.
22. Jackson P, Loughrey CM, Lightbody JH, McNamee PT, Young IS. Effect of hemodialysis on total antioxidant capacity and serum antioxidants in patients with chronic renal failure. Clin Chem 1995;41 (8 Pt 1):1135-8.
23. Kalk WJ, Morley JE, Gold CH, Meyers A. Thyroid function tests in patients on regular hemodialysis. Nephron 1980;25:173-8.
24. Ramirez G, O'Neill W Jr., Jubiz W, Bloomer HA. Thyroid dysfunction in uremia: Evidence for thyroid and hypophyseal abnormalities. Ann Intern Med 1976;84:672-6.
25. Annuk M, Zilmer M, Fellstro B. Endothelium-dependent vasodilation and oxidative stress in chronic renal failure: Impact on cardiovascular disease. Kidney Int 2003;63:50-3.
26. Freeman BA, Crapo JD. Biology of disease: Free radicals and tissue injury. Lab Invest 1982;47:412-26.
27. Dakshinamurty KV, Srinivasa Rao PV, Saibaba KS, Sheela RB, Venkataramana G, Shyam C, *et al*. Antioxidant status in patients on maintenance haemodialysis. Indian J Nephrol 2002;12:77-80.
28. Bloembergen WE, Port FK, Mauger EA, Wolfe RA. Causes of death in dialysis patients: Racial and gender differences. J Am Soc Nephrol 1994;5:1231-42.
29. Yeun JY, Levine RA, Mantadilok V, Kaysen GA. C-reactive protein predicts all-cause and cardiovascular mortality in hemodialysis patients. Am J Kidney Dis 2000;35:469-76.
30. Lowrie EG, Lew NL. Death risk in hemodialys patients: The predictive value of commonly measured variables and an evaluation of death rate differences between facilities. Am J Kidney Dis 1990;15:458-82.
31. Malyszko J, Malyszko JS, Pawlak K, Mysliwiec M. Thyroid function, endothelium, and inflammation in hemodialyzed patients: Possible relations? J Ren Nutr 2007;17:30-7.

32. Satoh K. Serum lipid peroxide in cerebrovascular disorders determined by a new colorimetric method. Clin Chim Acta 1978;90:37-43.
33. World Health Organization. Prevention and management of the global epidemic of obesity. Report of the WHO consultation on obesity. (Technical Report Series, No. 894). Geneva: WHO; 1998.
34. Spector DA, Davis PJ, Helderman JH, Bell B, Utiger RD. Thyroid function and metabolic state in chronic renal failure. Ann Intern Med 1976;85:724-30.
35. Lim VS, Fang VS, Katz AI, Refetoff S. Thyroid dysfunction in chronic renal failure. A study of the pituitary-thyroid axis and peripheral turnover kinetics of thyroxine and triiodothyronine. J Clin Invest 1977;60:522-34.
36. Kølendorf K, Møller BB, Rogowski P. The influence of chronic renal failure on serum and urinary thyroid hormone levels. Acta Endocrinol (Copenh) 1978;89:80-8.
37. Hershman JM, Krugman LG, Kopple JD, Reed AW, Azukizawa M, Shinaberger JH. Thyroid function in patients undergoing maintenance hemodialysis: Unexplained low serum thyroxine concentration. Metabolism 1978;27:755-9.
38. Gomez-Pan A, Alvarez-Ude F, Yeo PP, Hall R, Evered DC, Kerr DN. Function of the hypothalamo-hypophysial-thyroid axis in chronic renal failure. Clin Endocrinol (Oxf) 1979;11:567-74.
39. Forest JC, Dube J, Talbot J. Thyroid hormones in patients with chronic renal failure undergoing maintenance hemodialysis. Am J Clin Pathol 1982;77:580-6.
40. Hardy MJ, Ragbeer SS, Nascimento L. Pituitary-thyroid function in chronic renal failure assessed by a highly sensitive thyrotropin assay. J Clin Endocrinol Metab 1988;66:233-6.
41. Singh PA, Bobby Z, Selvaraj N, Vinayagamoorthi R. An evaluation of thyroid hormone status and oxidative stress in undialyzed chronic renal failure patients. Indian J Physiol Pharmacol 2006;50:279-84.
42. Rajagopalan B, Dolia PB, Arumalla VV, Seshadri Reddy V. Renal function markers and thyroid hormone status in undialyzed chronic kidney disease. Al Ameen J Med Sci 2013;6:70-4.
43. Sanai T, Okamura K, Kishi T, Miyazono M, Ikeda Y, Kitazono T. Importance of specific reference values for evaluation of the deteriorating thyroid function in patients with end-stage renal disease on hemodialysis. J Endocrinol Invest 2015;38:47-56.
44. Iglesias P, Díez JJ. Thyroid dysfunction and kidney disease. Eur J Endocrinol 2009;160:503-15.
45. Lin CC, Chen TW, Ng YY, Chou YH, Yang WC. Thyroid dysfunction and nodular goiter in hemodialysis and peritoneal dialysis patients. Perit Dial Int 1998;18:516-21.
46. Lo JC, Chertow GM, Go AS, Hsu CY. Increased prevalence of subclinical and clinical hypothyroidism in persons with chronic kidney disease. Kidney Int 2005;67:1047-52.
47. Kutlay S, Atli T, Koseogullari O, Nergizoglu G, Duman N, Gullu S. Thyroid disorders in hemodialysis patients in an iodine-deficient community. Artif Organs 2005;29:329-32.
48. Kang EW, Nam JY, Yoo TH, Shin SK, Kang SW, Han DS, *et al.* Clinical implications of subclinical hypothyroidism in continuous ambulatory peritoneal dialysis patients. Am J Nephrol 2008;28:908-13.
49. Targher G, Chonchol M, Zoppini G, Salvagno G, Pichiri I, Franchini M, *et al*. Prevalence of thyroid autoimmunity and subclinical hypothyroidism in persons with chronic kidney disease not requiring chronic dialysis. Clin Chem Lab Med 2009;47:1367-71.
50. Shantha GP, Kumar AA, Bhise V, Khanna R, Sivagnanam K, Subramanian KK. Prevalence of subclinical hypothyroidism in patients with end-stage renal disease and the role of serum albumin: A cross-sectional study from South India. Cardiorenal Med 2011;1:255-60.
51. Asvold BO, Bjøro T, Vatten LJ. Association of thyroid function with estimated glomerular filtration rate in a population-based study: The HUNT study. Eur J Endocrinol 2011;164:101-5.
52. Yonemura K, Nakajima T, Suzuki T, Ando S, Genma R, Nakamura H, *et al.* Low free thyroxine concentrations and deficient nocturnal surge of thyroid-stimulating hormone in haemodialysed patients compared with undialysed patients. Nephrol Dial Transplant 2000;15:668-72.
53. Lim VS, Henriquez C, Seo H, Refetoff S, Martino E. Thyroid function in a uremic rat model. Evidence suggesting tissue hypothyroidism. J Clin Invest 1980;66:946-54.
54. Lim VS, Passo C, Murata Y, Ferrari E, Nakamura H, Refetoff S. Reduced triiodothyronine content in liver but not pituitary of the uremic rat model: Demonstration of changes compatible with thyroid hormone deficiency in liver only. Endocrinology 1984;114:280-6.
55. Xess A, Gupta A, Kumar U, Sharma HP, Prasad KM. Evaluation of thyroid hormones in chronic renal failure. Indian J Pathol Microbiol 1999;42:129-33.
56. Voss P, Siems W. Clinical oxidation parameters of aging. Free Radic Res 2006;40:1339-49.
57. Valentini J, Grotto D, Paniz C, Roehrs M, Burg G, Garcia SC. The influence of the hemodialysis treatment time under oxidative stress biomarkers in chronic renal failure patients. Biomed Pharmacother 2008;62:378-82.
58. Massy ZA, Nguyen-Khoa T. Oxidative stress and chronic renal failure: Markers and management. J Nephrol 2002;15:336-41.
59. Fydryk J, Jacobson E, Kurzawska O, Malecka G, Gonet B, Urasinski T, *et al.* Antioxidant status of children with steroid-sensitive nephrotic syndrome. Pediatr Nephrol 1998;12:751-4.
60. Weinstein T, Chagnac A, Korzets A, Boaz M, Ori Y, Herman M, *et al.* Haemolysis in haemodialysis patients: Evidence for impaired defence mechanisms against oxidative stress. Nephrol Dial Transplant 2000;15:883-7.
61. Peuchant E, Carbonneau MA, Dubourg L, Thomas MJ, Perromat A, Vallot C, *et al.* Lipoperoxidation in plasma and red blood cells of patients undergoing haemodialysis: Vitamins A, E, and iron status. Free Radic Biol Med 1994;16:339-46.
62. Sawant BU, Nadkarni GD, Thakare UR, Joseph LJ, Rajan MG. Changes in lipid peroxidation and free radical scavengers in kidney of hypothyroid and hyperthyroid rats. Indian J Exp Biol 2003;41:1334-7.
63. Mimic-Oka J, Simic T, Djukanovic L, Reljic Z, Davicevic Z. Alteration in plasma antioxidant capacity in various degrees of chronic renal failure. Clin Nephrol 1999;51:233-41.
64. Mimic-Oka J, Simic T, Ekmescic V, Dragicevic P. Erythrocyte glutathione peroxidase and superoxide dismutase activities in different stages of chronic renal failure. Clin Nephrol 1995;44:44-8.
65. Dursun E, Ozben T, Süleymanlar G, Dursun B, Yakupoglu G. Effect of hemodialysis on the oxidative stress and antioxidants. Clin Chem Lab Med 2002;40:1009-13.
66. Konukoglu D, Ercan M, Ayaz M, Onen S. Plasma and erythrocytes antioxidant status and trace element levels in proteinuric patients with moderate glomerular function. J Trace Elem Med Biol 2001;15:119-22.
67. Nagase S, Aoyagi K, Hirayama A, Gotoh M, Ueda A, Tomida C, *et al.* Favorable effect of hemodialysis on decreased serum antioxidant activity in hemodialysis patients demonstrated by electron spin resonance. J Am Soc Nephrol 1997;8:1157-63.
68. Ozden M, Maral H, Akaydin D, Cetinalp P, Kalender B. Erythrocyte glutathione peroxidase activity, plasma malondialdehyde and erythrocyte glutathione levels in hemodialysis and CAPD patients. Clin Biochem 2002;35:269-73.
69. Vanella A, Geremia E, Pinturo R, Tiriolo P, Liuzzo G, Tiriolo C, *et al.* Superoxide dismutase activity and reduced glutathione content in erythrocytes of uremic patients on chronic dialysis. Acta Haematol 1983;70:312-5.
70. Shainkin-Kestenbaum R, Caruso C, Berlyne GM. Reduced superoxide

dismutase activity in erythrocytes of dialysis patients: A possible factor in the etiology of uremic anemia. Nephron 1990;55:251-3.
71. Durak I, Akyol O, Basesme E, Canbolat O, Kavutçu M. Reduced erythrocyte defense mechanisms against free radical toxicity in patients with chronic renal failure. Nephron 1994;66:76-80.
72. Túri S, Németh I, Vargha I, Matkovics B, Dobos E. Erythrocyte defense mechanisms against free oxygen radicals in haemodialysed uraemic children. Pediatr Nephrol 1991;5:179-83.
73. Kaptein EM, Quion-Verde H, Chooljian CJ, Tang WW, Friedman PE, Rodriquez HJ, *et al*. The thyroid in end-stage renal disease. Medicine (Baltimore) 1988;67:187-97.
74. Iervasi G, Pingitore A, Landi P, Raciti M, Ripoli A, Scarlattini M, *et al*. Low-T3 syndrome: A strong prognostic predictor of death in patients with heart disease. Circulation 2003;107:708-13.
75. Zoccali C, Mallamaci F, Tripepi G, Cutrupi S, Pizzini P. Low triiodothyronine and survival in end-stage renal disease. Kidney Int 2006;70:523-8.
76. Famag M. Evaluation of thyroid function status in hemodialysis patients. Kerbala J Med 2009;9:716-24.