Impact of serum uric acid on the aggravation of renal function; current knowledge and new concepts

Hamid Nasri[1], Parto Nasri[2], Azar Baradaran[3], Hamid Reza Baradaran-Ghahfarokhi[4], Milad Baradaran-Ghahfarokhi[5], Mahmoud Rafieian-Kopaie[6]*

[1.] Department of Internal Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
[2.] School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
[3.] Department of Pathology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
[4.] Baradaran Pathology Laboratory, Isfahan, Iran
[5.] Department of Medical Physics and Medical Engineering, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran
[6.] Medical Plants Research Center, Shahrekord University of Medical Sciences, Shahrekord, Iran
rafieian@yahoo.com

Abstract: After a prolonged time of inertia, in the last decade, much interest has been directed toward the uric acid due to the results from experimental investigations that reveal detrimental effects of uric acid on blood pressure and renal function. This review aimed to discuss the impact of serum uric acid on the aggravation of renal function.
[Nasri H, Nasri P, Baradaran A, Baradaran-Ghahfarokhi HR, Baradaran-Ghahfarokhi M, Rafieian-Kopaie M. **Impact of serum uric acid on the aggravation of renal function; current knowledge and new concepts.** *Life Sci J* 2014;11(12s):71-76]. (ISSN:1097-8135). http://www.lifesciencesite.com. 12

Keywords: Chemotherapy; Cisplatin; renal toxicity

1. Introduction

After a prolonged time of inertia, in the last decade, much interest has been directed toward the uric acid due to the results from experimental investigations that reveal detrimental effects of uric acid on blood pressure and renal function (1-4). Until current years, uric acid was defined in the background of an end-product of purine degradation and encountered only in gout arthropathy and, to a lesser extent, in renal function disturbance in individuals with longstanding gout. Uric acid is now more recognized as the end-product of an enzyme system which is a main source of vascular oxygen radicals, namely the xanthine oxidoreductase system (3-7). An elevated serum uric acid value is frequently encountered in individuals who are found having chronic kidney disease. Epidemiological investigations have identified a relationship between hyperuricemia and cardiovascular risk in the general population and in chronic kidney diseasepatients (4-10). In hemodialysis individuals, investigations have shown a relationship between uric acid levels and mortality too (11-17). The relationship of uric acid and decline in kidney function has been investigated in various investigations which included healthy individuals, patients with chronic kidney disease stages I-II, patients with diabetes, and individuals on peritoneal dialysis (1-4,18-22). Nevertheless evidence about this association in patients with advanced chronic kidney disease (stages IV-V) is insufficient, and the effect on time until start of dialysis has not been evaluated properly(1-4,18-22). Various experimental studies have detected unequivocal results in which elevated serum uric acid levels have led to increased oxidative stress and inflammation, renal function deterioration, propagation of atherosclerosis and higher blood pressure. Improvement in these risk factors subsequent administration of allopurinol, a xanthine oxidase inhibitor which lowers serum uric acid levels, enforces the hypothesis that hyperuricemia is related toharmful impacts (1-8).Chronic renal failure is accompanied by significant morbidity and mortality (23-33). Besides to well-known risk factors such as hypertension and diabetes(34-40), several “non-traditional” risk factors could contribute to the higher risk of morbidity and mortality in patients with chronic renal failure compared to the general population (41-54). One of them is hyperuricemia. Previous studies have revealed that uric acid can result to glomerular hypertension,activation of renin-angiotensinsystem, arteriolosclerosis, glomerular hypertrophy, elevatedrenal vascular resistance, reduced renal blood flow, glomerulosclerosis, and interstitial fibrosis by inducing endothelial dysfunction and oxidative stress addressing that uric acid could be a factor to kidney injury (1-8). Recently, it was detected that, uric acid is capable to activate NFκB in proximal tubular cells, and observation that lowering serum uric acid via a uricosuric agent increases $1,25(OH)_2D$ levels in humans with gout propose that uric acid inhibits 1-α hydroxylase activity.Subsequently, inhibition of 1-α hydroxylase by uric acid may inhace the secretion of parathormone, a condition that aggravate renal

function in patients with chronic renal failure(1-8). In a study on 60 patients with type II diabetes without a history of gout, we found a significant positive association between body mass index (BMI) and serum uric acid levels ($r = 0.428$, $P = 0.001$). After adjustment for weight, a significant positive association of serum uric acid with proportion of proteinuria was detected ($r = 0.47$, $P < 0.001$) too (4). Furthermore, the correlation of serum uric acid with level of blood pressure was significantly positive (8). Subsequently, Jalalzadehet al., conducted a single-blind, randomized cross-over clinical study consisting 55 hemodialysis patients with serum uric acid level >6.5 (men) and >5.5 mg/dl (women) (55). They detected the a reduction of blood pressure by allopurinol treatment in hemodialysis patients (55). Moreover, Chen et al, in an in-vivo study on rats, found uric acid suppresses 1 alpha hydroxylase in vitro and in vivo(56). In fact, a reduction in 1,25(OH)2D secondary to reduced 1-α hydroxylase enzyme activity contributes to the development of secondary hyperparathyroidism in patients with chronic kidney disease as mentioned above too(57-60). Indeed, the direct association of hyperuricemia and vitamin D metabolism has two results. Firstly it is well understand that hyperuricemia by itself is an independent risk factor for kidney damage in various renal disease, like IgA nephritis or diabetic nephropathy(57-65). Many studies, support the hypothesis that elevated serum uric acid levels have an injurious effect, resulting to inflammation, endothelial dysfunction and vascular disease ().Secondly, regardless of the deleterious effect of hyperuricemia on hypertension and aggravation of some type of nephropathies, its harmful effect on vitamin D production is of significant importance (57-67). Various studies had shown,supports vitamin D as a negative regulator of the circulating and local tissue renin-angiotensin system, while renin-angiotensin system has a critical implication in the physiology of sodium and volume homeostasis. Thus, excess activity of renin-angiotensin system is associated with high blood pressure, aggravation of renal disease and diabetic kidney disease (57-68).

Some factors regulate the uric acid in the chronic renal disease patient. Dietary intake of purines and fructose is a primary source of uric acid.Hence, its levels could vary with the nutritional status. While the kidney eliminates much of the generated uric acid, a decrease in renal function is associated with an increase in blood uric acidlevels. Upon reaction of uric acid with oxidants, it will undergo degradation to allantoin and other products. In the chronic kidney disease patients, this degradation pathway is augmented five-fold or more (1-10). Studies regarding uric acid and start of dialysis have shown that, high uric acid levels at baseline were associated with a shorter time until initiate of dialysis. On the other hand, gout is caused by deposition of uric acid crystals in the joints, most notably in the metatarsal-interphalangeal joint of the big toe. Painful and disabling symptoms of gout arthritis could have contributed to the decision of the physician and patient to start dialysis (1-10). In addition, another explanation could be that high levels of uric acid might have resulted in other symptoms or clinical conditions such as renal stones or hypertension that affect the decision to start dialysis (1-10). In fact, higher uric acid levels in incident pre-dialysis patients are a risk factor for an early initiate of dialysis. Indeed, studies some studies indicated that patients with higher uric acid levels should be referred earlier to pre-dialysis care in order to guarantee appropriate preparation for beginning of dialysis (69-75). It is possible that serum uric acid levels,may be a guide for nephrologists to assess the optimal moment to start dialysis, while some studies have established that higher baseline uric acid levels lead to an earlier start of dialysis, independent of other factors (1-9). Since various investigations have assessed whether allopurinol could prevent or at least slow the progression of renal disease. It is possible that, early treatment of patients with familial juvenile hyperuricemic nephropathy with allopurinol diminished the morbidity and mortality from renal failure as compared with their untreated siblings and previous generations of recruited families (1-0,76-84). Additionally in hyperuricemicpatients with chronic renal failure, who received allopurinol, dosed at 100-300 mg/day, or usual therapy for 12 months, a trend toward a lower serum creatinine level in the treatment group compared with controls at study completion, though this difference did not reach statistical significance (2-9). Additionally, various clinical studies have detected that, lowering uric acid with allopurinol ameliorated endothelial dysfunction in both hyperuricemic individuals and hypertensive type II diabetic patients with normal serum uric acid levels too (3-11,85-108). The suggested mechanism is that elevated serum uric acid levels causes endothelial dysfunction by activating the renin–angiotensin system,inhibiting nitric oxide synthetase and causing pro-inflammation and resultant endothelial dysfunction, and vascular smooth muscle cell, and finally contributing to atherothrombosis (1-10). In the meantime,further clinical studies are warranted to elucidate the beneficial effect of allopurinol therapy in nephropathies.

Corresponding Author:
Prof. Mahmoud Rafieian-Kopaei
Medical Plants Research Center
Shahrekord University of Medical Sciences
Shahrekord, Iran
Email: rafieian@yahoo.com

References

1. Nasri H. Commentary on: Is uric acid an indicator of metabolic syndrome in the first-degree relatives of patients with type 2 diabetes? J Res Med Sci. 2013; 18(3):267-8.
2. Nasri H, Rafieian-Kopaei M. Hyperuricemia; a new look at an old problem. J Nephropharmacol 2012;1(2):13-14.
3. Pickering JW, Endre ZH. The definition and detection of acute kidney injury. J Renal Inj Prev 2014; 3(1):21-25.
4. Behradmanesh S, Horestani MK, Baradaran A, Nasri H. Association of serum uric acid with proteinuria in type 2 diabetic patients.J Res Med Sci. 2013;18(1):44-6.
5. Gheissari A. Acute kidney injury and renal angina. J Renal InjPrev 2013; 2(2): 33-34.
6. Spasovski D. Renal markers for assessment of renal tubular and glomerular dysfunction. J Nephropharmacol 2013; 2(2):23-25.
7. Hernandez GT, Nasri H. World Kidney Day 2014: increasing awareness of chronic kidney disease and aging. J Renal Inj Prev 2014; 3(1):3-4.
8. Rafieian-Kopaei M, Behradmanesh S, Kheiri S, Nasri H. Association of serum uric Acid with level of blood pressure in type 2 diabetic patients. Iran J Kidney Dis. 2014; 8(2):152-4.
9. Nasri H, Ardalan MR. Significance of hyperuricemia in immunoglobulin A nephropathy. J Renal Inj Prev 2013; 2(3): 105-106.
10. Momeni A. Serum uric acid and diabetic nephropathy. J Renal Inj Prev 2012; 1(1): 37-38.
11. Nasri H.Serum C-reactive protein (CRP) in association with various nutritional parameters in maintenance hemodialysispatients. Bratisl Lek Listy. 2005; 106(12):390-5.
12. Nasri H. Association of Ca×PO4 product with levels of serum C-reactive protein in regular hemodialysis patients. J Renal Inj Prev 2012; 1(2):55-59.
13. N. The association between serum leptin and blood lymphocytes in hemodialysis patients. Bratisl LekListy. 2007;108(3):122-7.
14. Gheissari A, Mehrasa P, Merrikhi A, Madihi Y. Acute kidney injury: A pediatric experience over 10 years at a tertiary care center. J Nephropathol. 2012;1(2):101-8.
15. Kang DH, Nakagawa T, Feng L, Watanabe S, Han L, Mazzali M, et al. A role for uric acid in the progression of renal disease. J Am Soc Nephrol. 2002; 13:2888–97.
16. Nasri H. World kidney day 2013: acute kidney injury; a public health aware. Iran J Public Health. 2013 Mar 1;42(3):338-40.
17. Hajivandi A, Amiri M. World diabetes day: diabetes mellitus and nephrology. J Nephropharmacol. 2013; 2(2):31-32.
18. Tamadon MR. Secondary hyperparathyroidism and chronic kidney disease. J Parathyr Dis 2013; 1(1):15-16.
19. Assadi F. The epidemic of pediatric chronic kidney disease: The danger of skepticism. J Nephropathol. 2012; 1:61–4.
20. Tamadon MR, Ardalan MR, Nasri H. World Kidney Day 2013; acute renal injury; a global health warning. J Parathyr Dis 2013;1(2):27-28.
21. N, YazdaniM. The relationship between serum LDL-cholesterol, HDL-cholesterol and systolic blood pressure in patients with type 2 diabetes. Kardiol Pol. 2006; 64(12):1364-8.
22. Hajivandi A, Amiri M. World Kidney Day 2014: Kidney disease and elderly. J Parathyr Dis 2014; 2(1):3-4.
23. Nasri H, Baradaran A, Doroudgar F, Ganji F. Relationship of conjunctival and corneal calcification with secondary hyperparathyroidism in hemodialysis patients. Iran J Med Sci 2003; 28(2):86-9.
24. Ghorbani A, Jasemi-Zergani F. Ticlopidine to prevent primary arteriovenous fistula failure in hemodialysis patients; a randomized controlled trial. J Renal Inj Prev 2013; 2(3): 109-111.
25. Gheissari A, Hemmatzadeh S, Merrikhi A, Fadaei Tehrani S, Madihi Y. Chronic kidney disease in children: A report from a tertiary care center over 11 years. J Nephropathol. 2012;1(3):177-82.
26. N, Baradaran A. Association of serum lipoprotein (a) with ultrasonographically determined early atherosclerotic changes in the carotid and femoral arteries in kidney transplanted patients.Transplant Proc. 2004;36(9):2683-6.
27. Shahbazian H. World diabetes day; 2013. J Renal Inj Prev 2013; 2(4): 123-124.
28. Nasri H, Baradaran A. Correlation of serum magnesium with dyslipidemia in maintenance hemodialysis patients. Acta Medica (Hradec Kralove). 2004;47(4):263-5.
29. Behradmanesh S, Derees F, Rafieian-kopaei M. Effect of *Salvia officinalis* on diabetic patients. J Renal Inj Prev 2013; 2(2): 51-54.
30. Kari J. Epidemiology of chronic kidney disease in children. J Nephropathol. 2012;1(3):162-3.
31. Nasri H. Serum C-reactive protein (CRP) in association with various nutritional parameters in maintenance hemodialysis patients. Bratisl Lek Listy. 2005;106(12):390-5.
32. Behradmanesh S, Nasri P. Serum cholesterol and LDL-C in association with level of diastolic blood pressure in type 2 diabetic patients. J Renal Inj Prev 2012; 1(1): 23-26.

33. Nasri, H., S. Shirani. Baradaran A. Lipids in association with leptin in maintenance hemodialysis patients. J Med Sci.2006; 6: 173-179.
34. Rafieian-Kopaei M, Nasri H. Carotid intima-media thickness and left ventricular hypertrophy in hemodialysis patients. J Renal Inj Prev 2013; 2(4): 129-132.
35. A, NasriH. Prevalence of Helicobacter pylori infection in maintenance hemodialysis patients with non-ulcer dyspepsia. Saudi J Kidney Dis Transpl. 2009;20(2):223-6.
36. Nasri H, Behradmanesh S, Ahmadi A, Baradaran A, Nasri P, Rafieian-Kopaei M. Association of serum lipids with level of blood pressure in type 2 diabetic patients. J Renal Inj Prev 2014; 3(2):43-46.
37. Ghorbani A, Jasemi-Zergani F. Ticlopidine to prevent primary arteriovenous fistula failure in hemodialysis patients; a randomized controlled trial. J Renal Inj Prev 2013; 2(3): 109-111.
38. N, Kheiri S. Effects of diabetes mellitus, age, and duration of dialysis on parathormone in chronic hemodialysis patients. Saudi J Kidney Dis Transpl. 2008;19(4):608-13.
39. Rafieian-Kopaei M, Nasri H. Serum lipoprotein (a) and atherosclerotic changes in hemodialysis patients. J Renal Inj Prev 2013; 2(2): 47-50.
40. N. Association of serum lipoprotein (a) with hypertension in diabetic patients. Saudi J Kidney Dis Transpl. 2008;19(3):420-7.
41. Solati M, Mahboobi HR. Paraoxonase enzyme activity and dyslipidemia in chronic kidney disease patients. J Nephropathol. 2012;1(3):123-5.
42. N. Linkage of elevated CaxPO4 product with inflammation in maintenance hemodialysis patients. Minerva Urol Nefrol. 2006;58(4):339-45.
43. Rahimi Z. ACE insertion/deletion (I/D) polymorphism and diabetic nephropathy. J Nephropathol 2012; 1: 143-151
44. N. Serum leptin concentration and left ventricular hypertrophy and function in maintenance hemodialysis patients. Minerva Urol Nefrol. 2006;58(2):189-93.
45. Rahimi Z, Mansouri Zaveleh O, Rahimi Z, Abbasi A. AT2R-1332 G:A polymorphism and diabetic nephropathy in type 2 diabetes mellitus patients. J Renal Inj Prev 2013; 2: 97-101.
46. Nasri H. Pulmonary artery pressure in association with serum parathormone in maintenance hemodialysis patients. Arch Med Sci 2006; 2(1):32-5. 47-Baradaran A. Lipoprotein(a), type 2 diabetes and nephropathy; the mystery continues. J Nephropathol. 2012;1(3):126-9.
47. Nasri H. The awareness of chronic kidney disease and aging; the focus of world kidney day in 2014. J Nephropharmacol 2014; 3(1):1-2.
48. Tamadon MR, Baradaran A, Rafieian-Kopaei M. Antioxidant and kidney protection; differential impacts of single and whole natural antioxidants. J Renal Inj Prev 2014; 3(2):41-42.
49. Nasri H, Mubarak M. Contrast induced nephropathy has to be differentiated from kidney injury due to atheroembolic disease. J Renal Inj Prev 2012; 2(3): 107-108.
50. Rouhi H, Ganji F.Effects of N-acetyl cysteine on serum lipoprotein (a) and proteinuria in type 2 diabetic patients. J Nephropathol. 2013;2(1):61-6.
51. N. Helicobacter pylori infection and its relationship to plasma magnesium in hemodialysis patients. Bratisl Lek Listy. 2007;108(12):506-9.
52. Tamadon MR, Beladi-Mousavi SS. Erythropoietin; a review on current knowledge and new concepts. J Renal Inj Prev 2013; 2(4): 119-121.
53. N, Baradaran A. The influence of serum 25-hydroxy vitamin D levels on Helicobacter Pylori Infections in patients with end-stage renal failure on regular hemodialysis. Saudi J Kidney Dis Transpl. 2007;18(2):215-9.
54. Jalalzadeh M, Nurcheshmeh Z, Mohammadi R, Mousavinasab N, Ghadiani MH. The effect of allopurinol on lowering blood pressure in hemodialysis patients with hyperuricemia.J Res Med Sci. 2012; 17(11):1039-46.
55. C, Roncal-Jimenez C, Lanaspa M, Gerard S, Chonchol M, Johnson RJ, et al. Uric acid suppresses 1 alpha hydroxylase in vitro and in vivo. Metabolism. 2014; 63(1):150-60.
56. B, Behradmanesh S, Nasri H. Association of body mass index and serum vitamin D level in healthy Iranian adolescents. Endokrynol Pol. 2012;63(1):29-33.
57. Rafieian-Kopaei M, Nasri H. Vitamin D therapy in diabetic kidney disease. J Nephropharmacol 2014; 3(1):3-4.
58. Ardalan MR, Sanadgol H, Nasri H, Baradaran A, Tamadon MR, Rafieian-Kopaei R. Vitamin D therapy in diabetic kidney disease; current knowledge on a public health problem. J Parathyr Dis 2014; 2(1):15-17.
59. Nasri H, Rafieian-Kopaei M. Association of serum vitamin D level with age in individuals with normal renal function. J Nephropharmacol. 2012;1(1):7–9.
60. Nasri H. Correlation of serum magnesium with serum levels of 25-hydroxyvitamin D in hemodialysis patients. J Parathyr Dis 2014; 2(1):11-13.
61. Ardalan MR, Sanadgol H, Nasri H, Baradaran A, Tamadon MR, Rafieian-Kopaei R. Impact of vitamin D on the immune system in kidney disease. J Parathyr Dis 2013; 1(2):17-20.
62. Ajabshir S, Asif A, NayerA. The effects of vitamin D on the renin-angiotensin system. J Nephropathol. 2014;3(2):41-3.
63. Nasri H, Behradmanesh S, Maghsoudi AR, Ahmadi A, Nasri P, Rafieian-Kopaei M. Efficacy of supplementary vitamin D on improvement of glycemic parameters in patients with type 2 diabetes mellitus; a randomized double blind clinical trial. J Renal Inj Prev 2014; 3(1):31-34.

64. N, Baradaran A.The influence of serum 25-hydroxy vitamin D levels on Helicobacter Pylori Infections in patients with end-stage renal failure on regular hemodialysis. Saudi J Kidney Dis Transpl. 2007;18(2):215-9.
65. Nasri H, Rafieian-Kopaei M. Significant difference of serum 25-hydroxyvitamin D level in male hemodialysis patients with our without diabetes; a single center study. J Nephropharmacol. 2012;1(2):3–4.
66. Nasri H, Behradmanesh S, Ahmadi A, Rafieian-Kopaei M. Impact of oral vitamin D (cholecalciferol) replacement therapy on blood pressure in type 2 diabetes patients; a randomized, double- blind, placebo controlled clinical trial. J Nephropathol. 2014; 3(1): 29-33.
67. Baradaran A. Beyond mineral metabolism, the bright immunomodulatory effect of vitamin D in renal disease. J Nephropharmacol 2012;1(2):17-18.
68. Khosla UM, Zharikov S, Finch JL, Nakagawa T, Roncal C, Mu W, et al. Hyperuricemia induces endothelial dysfunction. Kidney Int. 2005; 67:1739–42.
69. Amiri M, Nasri H. Secondary Hyperparathyroidism in chronic kidney disease patients; current knowledge. J Parathyr Dis 2014; 2(1):1-2.
70. Mowlaie M, Nasri H. Close association of arterial plaques with left ventricular hypertrophy and ejection fraction in hemodialysis patients. J Nephropharmacol.2014; 3(1):9-12.
71. Salehidoost R, Aminorroayai A, Zare M, Amini M. Is uric acid an indicator of metabolic syndrome in the first-degree relatives of patients with type 2 diabetes? J Res Med Sci. 2012;17:1005–10.
72. Tavafi M. Diabetic nephropathy and antioxidants. J Nephropathol. 2013;2:20–7.
73. Nasri H. Association of Ca×PO4 product with levels of serum C-reactive protein in regular hemodialysis patients. J Renal Inj Prev 2012; 1(2):55-59.
74. Nasri H, Sahinfard N, Rafieian M, Rafieian S, Shirzad M, Rafieian-kopaei M. Effects of *Allium sativum* on liver enzymes and atherosclerotic risk factors. J HerbMed Pharmacol. 2013; 2(2): 23-28
75. Jalal DI, Maahs DM, Hovind P, Nakagawa T. Uric acid as a mediator of diabetic nephropathy. Semin Nephrol. 2011;31:459–65.
76. Ali Alavian-Ghavanini, Milad Baradaran-Ghahfarokhi. Comment on: MTT assay instead of the clonogenic assay in measuring the response of cells to ionizing radiation. J Radiobiol. 2014;1(1):15-16.
77. B, Behradmanesh S, NasriH. Association of body mass index and serum vitamin D level in healthy Iranian adolescents. Endokrynol Pol. 2012;63(1):29-33.
78. Baldwin WM, Marek G, Wymer D, Pannu V, Baylis C, Johnson RJ, et al. Hyperuricemia as a Mediator of the Proinflammatory Endocrine Imbalance in the Adipose Tissue in a Murine Model of the Metabolic Syndrome. Diabetes. 2011;60:1258–69.
79. Nasri H. Elevated serum parathyroid hormone is a heart risk factor in hemodialysis patients. J Parathyr Dis 2013; 1(1):13-14.
80. N, Nematbakhsh M, Ghobadi S, Ansari R, Shahinfard N, Rafieian-Kopaei M. Preventive and curative effects of ginger extract against histopathologic changes of gentamicin-induced tubular toxicity in rats. Int J Prev Med. 2013;4(3):316-21.
81. Doria A, Krolewski AS. Diabetes: Lowering serum uric acid levels to prevent kidney failure. Nat Rev Nephrol. 2011; 7:495–6.
82. Sedighi M, Nasri H, Rafieian-kopaei M, Mortazaei S. Reversal effect of Achillea millefolium extract on ileum contractions. J Herb Med Pharmacol. 2013; 2(1): 5-8
83. Rastegari E, Nasri H. Association of serum leptin with serum C-reactive protein in hemodialysis patients. J Nephropharmacol 2012;1(2):19-21.
84. Rafieian-Kopaei M. Medicinal plants and the human needs. J HerbMed Plarmacol. 2012; 1(1):1-2.
85. Baradaran A, Rabiei Z, Rafieian M, Shirzad H. A review study on medicinal plants affecting amnesia through cholinergic system. J HerbMed Plarmacol. 2012; 1(1): 3-9.
86. B, Nasri H.Correlation of serum magnesium with serum parathormone levels in patients on regular hemodialysis. Saudi J Kidney Dis Transpl. 2006;17(3):344-50.
87. Ansari R, Shahinfard N, Namjou A, Rafieian M, Shirzad H, Rafieian-kopaei M. Ameliorative property of Teucrium polium on second degree burn. J HerbMed Plarmacol. 2013; 2(1): 9-11.
88. A, Kelishadi R, Rafieian-Kopaei M, Najafi S, Najafi M, Sahebkar A. Investigation of the lipid-modifying and antiinflammatory effects of Cornus mas L. supplementation on dyslipidemic children and adolescents. Pediatr Cardiol. 2013;34(7):1729-35.
89. Bahmani M, Vakili-Saatloo N, Gholami-Ahangaran M, Karamati SA, Khalil-Banihabib E, Hajigholizadeh Gh, et al. A comparison study on the anti-leech effects of onion (Allium cepa L) and ginger (Zingiber officinale) with levamisole and triclabendazole. J HerbMed Pharmacol. 2013; 2(1): 1-3.
90. H, Nematbakhsh M, Talebi A, Nasri H, Ashrafi F, Roshanaei K, Eshraghi-Jazi F, Pezeshki Z, Safari T.The role of angiotensin II receptor 1 (AT1) blockade in cisplatin-induced nephrotoxicity in rats: gender-related differences. Ren Fail. 2012; 34(8):1046-51.
91. Bahmani M, Vakili-Saatloo N, Maghsoudi R, Momtaz H, Saki K, Kazemi-Ghoshchi B, et al. A comparative study on the effect of ethanol extract

of wild Scrophularia deserti and streptomycin on Brucellla melitensis. J Herb Med Pharmacol.2013; 2(1): 17-20
92. Shirzad H, Kiani M, Shirzad M. Impacts of tomato extract on the mice fibrosarcoma cells. J HerbMed Pharmacol. 2013; 2(1): 13-6.
93. N, Ashrafi F, Safari T, Talebi A, Nasri H, Mortazavi M, Khazaei M, Baradaran-Mahdavi MM. Administration of vitamin E and losartan as prophylaxes in cisplatin-induced nephrotoxicity model in rats. J Nephrol. 2012;25(3):410-7.
94. Nasri H, Shirzad H. Toxicity and safety of medicinal plants. J HerbMed Plarmacol. 2013; 2(2): 21-22.
95. Namjoo AR, MirVakili M, Shirzad H, Faghani M. Biochemical, liver and renal toxicities of Melissa officinals hydroalcoholic extract on balb/C mice. J HerbMed Pharmacol. 2013; 2(2): 35-40.
96. Asgary S, Keshvari M, Sahebkar A, Hashemi M, Rafieian-Kopaei. Clinical investigation of the acute effects of pomegranate juice on blood pressure and endothelial function in hypertensive individuals. ARYA Atheroscler 2013; 9(6): 326-31.
97. K, MohammadifardN, Sarrafzadegan N, Sajjadi F, Maghroun M, Khosravi A, Alikhasi H, Rafieian M, Azadbakht L. Potato consumption and cardiovascular disease risk factors among Iranian population. Int J Food Sci Nutr. 2012; 63(8):913-20.
98. K, Sarrafzadegan N, Mohammadifard N, Sajjadi F, Maghroun M, Asgari S, Rafieian-Kopaei M, Azadbakht L. White rice consumption and CVD risk factors among Iranian population. J Health Popul Nutr. 2013;31(2):252-61.
99. Asgary S, Rafieian-Kopaei M, Najafi S, Heidarian E, Sahebkar A. Antihyperlipidemic effects of Sesamum indicum L. in rabbits fed a high-fat diet. The Scientific World Journal. 2013, Article ID 365892, 5: 1-4.
100. Shahbazi-Gahrouei D, Baradaran-Ghahfarokhi M. Assessment of entrance surface dose and health risk from common radiology examinations in Iran. Radiat Prot Dosimetry. 2013;154(3):308-13.
101. Baradaran-Ghahfarokhi M. Normal tissue complication probability modeling of radiation-induced bladder complications. J Radiobiol. 2014;1(1):19-20.
102. Hematti S, Baradaran-Ghahfarokhi M, Khajooei-Fard R, Mohammadi-Bertiani Z. Spiritual Well-Being for Increasing Life Expectancy in Palliative Radiotherapy Patients: A Questionnaire-Based Study. J Relig Health. 2014. (doi: 10.1007/s10943-014-9872-9).
103. Shokrani P, Baradaran-Ghahfarokhi M, Zadeh MK. A novel approach in electron beam radiation therapy of lips carcinoma: a Monte Carlo study. Med Phys. 2013;40(4):041720.
104. Shahbazi-Gahrouei D, Karbalae M, Moradi HA, Baradaran-Ghahfarokhi M. Health effects of living near mobile phone base transceiver station (BTS) antennae: a report from Isfahan, Iran. Electromagn Biol Med. 2013.
105. doi: 10.3109/15368378.2013.801352)
106. Khosravi, M., Shahbazi-Gahrouei, D., Jabbari, K., Nasri-Nasrabadi, M., Baradaran-Ghahfarokhi, M., Siavashpour, Z., Gheisari, R., Amiri, B. Photoneutron contamination from an 18 MV saturne medical linear accelerator in the treatment room. Radiat Prot Dosimetry 2013;156 (3):356-363.
107. Lotfi, M., Bagheri, M.H., Mosleh-Shirazi, M.A., Faghihi, R., Baradaran-Ghahfarokhi, M. Evaluation of the changes in the shape and location of the prostate and pelvic organs due to bladder filling and rectal distension. Iranian Red Crescent Medical Journal 2011; 13 (8):51-60.
108. Shahbazi-Gahrouei D. Radiobiological modeling in radiation oncology. J Radiobiol. 2014;1(1):17-18.
109. Safora Nikzad, Bijan Hashemi. MTT assay instead of the clonogenic assay in measuring the response of cells to ionizing radiation. J Radiobiol. 2014;1(1):3-8.

7/19/2014