Original Paper

# The Effect of Intravenous vitamin C on Ferritin Levels in Patients Hemodialysis Patients, A Clinical Trial

Sepideh Hajian,[1] Mohammad Taheri,[2] Navid Mohammadi[3,4]

[1]Department of Nephrology, Velayat Hospital, Qazvin University of medical sciences, Qazvin, Iran
[2]Qazvin University of medical sciences, Qazvin, Iran
[3]Children Growth Research Center, Research Institute for Prevention of Non-Communicable Diseases, Qazvin University of Medical Sciences, Qazvin, Iran
[4]Canada Optimax Access Consultation, Ottawa, Canada

**Keywords.** ascorbic acid, vitamin C, ferritins, hemodialysis, chronic kidney failure

**Introduction.** Administration of intravenous vitamin C in hemodialysis patients can reduce their ferritin levels. Nevertheless, little research has been carried out in this regard. Hence, this study aimed to determine the effect of intravenous vitamin C on ferritin levels in a group of hemodialysis patients.
**Methods.** The study population included 32 patients with chronic renal failure undergoing hemodialysis who had been referred to Qazvin Hospital. These patients had functional iron deficiency (IDA) and high levels of serum ferritin. Patients were randomly allocated into intervention group A (n = 16) and control group B (n = 16). Group A was given intravenous ascorbic acid, while group B was given the same amount of distilled water as a placebo three times a week after each dialysis session for three months along with erythropoietin. Laboratory parameters were assessed at the beginning and the end in an interval of three months.
**Results.** In patients who received vitamin C injections, the mean ferritin level decreased at the end of the study ($P < .05$). But vitamin C intake did not affect BUN, creatinine, sodium, potassium, TIBC, hemoglobin, platelets count, and the length and number of dialysis sessions.
**Conclusion.** Results of our study showed that vitamin C can reduce serum ferritin levels in hemodialysis patients. Therefore, it can be used as an adjunct in the treatment of anemia in patients.

IJKD 2022;16:6-12
www.ijkd.org
DOI: 10.52547/ijkd.6531

## INTRODUCTION

Chronic kidney disease (CKD) is a condition characterized by a gradual decrease in the renal function to purify the blood. Albuminuria is one of the diagnostic hallmarks of CKD. As a result of reduced urine output in long term, excess fluids build up and wastes accumulate in the body. Bone complications and anemia are not far-fetched in CKD when the patients are predisposed by underlying diseases such as diabetes, hypertension, and cardiovascular diseases. Excessive excretion of proteins along with the accumulation of excess fluids and toxins in the body are associated with edema and swelling, especially in the lower extremities. Furthermore, the patients with CKD manifest fatigue, vomiting, and loss of appetite.[1]

Dialysis is a procedure where filtering membranes of a dialysis machine purify the blood to restore the homeostasis and the balance of water and electrolytes. Both hemodialysis and peritoneal dialysis, pose clinical challenges for patients and nephrologists, despite their positive effects on increasing life expectancy. Long-term use of hemodialysis machine causes discomfort for the patient and various complications such as hemolysis and loss of blood cells while passing through the membrane filters.[2] Hemolysis itself causes anemia mainly through impairment of the production of erythropoietin (EPO) and lose of the ability to transfer the body's iron storage to hemoglobin, and hence a reduction in erythrocyte regeneration. Accumulation of uric acid as a result of its reduced urine excretion may also suppress bone marrow and intensify the malfunctioned cycle of red blood cell production.[3,4] To resolve the problem, physicians used stimulants to induce the production of red blood cells. However, the use of erythropoietin-stimulating agents (ESAs) was shown to be associated with exacerbation of cardiovascular events and cancers.[5] Afterward, treatments have been shifted to the use of iron supplements and blood transfusions. Although iron supplements reduce the need for erythropoietin, they cause iron overload, which may be associated with iron deposition in the liver and bone marrow.

Iron ions are absorbed in the form of ferrous by intestinal cells. Then, they bind to the iron-transporting protein (transferrin) in the form of ferric to reach the target organs. Bone marrow and other tissues involved in red blood cell production utilize ferrous iron to produce hemoglobin. Excess iron ions are then stored as ferric in the ferritin.[6] Ferritin is the major protein that stores iron and releases it. Ferritin is also a well-known inflammatory marker, and a concomitant inflammatory state in CKD patients along with the state of iron overload in the body leads to an excess of ferritin level. Hence, excess ferritin damages organs such as the heart, brain, joints, and bone marrow.[7,8] Studies have shown that vitamin C (also known as ascorbic acid) increases the absorption of iron from the intestine, facilitates the release of iron from ferritin, and enhances iron access for erythropoiesis. The antioxidant properties of ascorbic acid accelerate the conversion of ferric iron to the ferrous form. Given these facts, positive effects of vitamin C may be argued in patients with chronic renal failure undergoing dialysis.

However, complications such as oxalosis (defined as deposition of oxalate crystals in the kidney), prooxidant-induced stress, the possible hemolysis due to vitamin C prescription in patients with glucose 6-phosphate dehydrogenase deficiency, altered lymphocyte activity, acid-base disorder, and increased level of serum sodium, are still concerned following vitamin C consumption [9-11]. In general, studies have shown that intravenous vitamin C can reduce ferritin levels in patients with renal failure undergoing hemodialysis; however, there is a paucity of knowledge.[12,13] On the other hand, venofer (iron sucrose) injection is contraindicated in patients with ferritin levels of more than 500 microgram/liter and puts an economic burden on patients who can receive it. Therefore, this study aimed to determine the effect of vitamin C on ferritin levels in hemodialysis patients.

## MATERIALS AND METHODS

This clinical trial evaluated the effects of intravenous vitamin C on ferritin levels in patients with renal failure undergoing hemodialysis at Qazvin Velayat Hospital during the year 2019. The study was approved by the ethics committee of Qazvin University of Medical Sciences and received a clinical trial code (IRCT20191112045426N1). The confidentiality and privacy of personal data obtained from participating patients were kept. Considering a type one error of 0.05 and type 2 error of 0.2 and using the G*Power 3.1.9.2 software, the sample size was measured and 32 patients undergoing hemodialysis were enrolled in the trial.

Inclusion criteria were iron deficiency anemia in hemodialysis patients, a mean Hb < 11 g/dL 7, serum ferritin level (> 500 ng/mL), and transferrin saturation (TS) ≤ 20%. Patients were excluded from the study if they had a history of injection of venofer in the last two months, if they had an inflammatory disease, or if they were unwilling to participate or continue the trial. Study procedures and their objectives were thoroughly explained to the participants, and written consent was obtained. Using the WinPepi software, patients were randomly divided into intervention groups (A) (n = 16) and control groups (B) (n = 16). In this project, the patients and the researchers who administered the intervention and those who evaluated the results were blinded to patients' allocation and the type of intervention prescribed; hence, the study was conducted in a triple-blind pattern.

Along with intravenous erythropoietin, group A was given 500 mg intravenous ascorbic acid three times a week after each dialysis session for three months. On the other hand, group B was given the same amount of distilled water as placebo along with intravenous erythropoietin during this period. Both the placebo and vitamin C were administered in the same-sized syringes to the patients. Serum levels of ferritin, hemoglobin, total iron-binding capacity (TIBC), and the transferrin saturation percentage (TSAT) in all participants were measured at the beginning and the end of the study. Demographic characteristics such as age, sex, marital status at the time of the study were also recorded.

Quantitative data were described using mean and standard deviation, and qualitative data were described using frequency and percentage. An independent t-test was used to analyze the quantitative variables with normal distribution and the Mann-Whitney U test for the data with skewed distribution. The Chi-square test was employed to compare qualitative variables between the two groups. The effect of vitamin C on ferritin levels was calculated in both groups. Logistic regression equation was used to investigate the factors affecting a qualitative variable.

## RESULTS

A total of 32 patients participated in this study, of whom 16 received intravenous ascorbic acid (intervention group) and 16 did not (control group). The distribution of gender and marital status were not significantly different between the two groups ($P > .05$) and therefore, did not bias the obtained results. Table 1 shows other demographic characteristics of the studied population.

Table 2 shows the mean levels of BUN (mg/

**Table 1.** Distribution of Demographic Data in Patients with Renal Failure Undergoing Hemodialysis

| | Intervention Group | Control Group | Total |
|---|---|---|---|
| Male (%) | 7 (43.8) | 11 (68.8) | 18 (56.3) |
| Female (%) | 9 (56.3) | 5 (31.3) | 14 (43.8) |
| Single (%) | 0 | 2 (12.5) | 2 (6.3) |
| Married (%) | 16 (100) | 14 (87.5) | 30 (93.8) |
| Mean Age, y | 60.94 | 49.69 | 55.3 |
| Age Standard Deviation, y | 14.29 | 21.82 | 19.02 |
| Minimum Age, y | 30 | 9 | 9 |
| Maximum Age, y | 81 | 83 | 83 |
| Mean Weight, kg | 69.81 | 61.81 | 65.81 |
| Weight Standard Deviation, kg | 12.37 | 15.38 | 14.32 |
| Minimum Weight, kg | 45 | 27 | 27 |
| Maximum Weight, kg | 85 | 90 | 90 |

**Table 2.** Mean BUN (mg/dL), Cr (mg/dL), Na (mmol/L), K (mmol/L), Hb (g/dL), Plt (*10³) in Patients with Renal Failure Undergoing Hemodialysis at the Beginning and at the End of the Study

| | The Beginning of the Study | | | The End of the Study | | | *P* |
|---|---|---|---|---|---|---|---|
| | Mean ( ± SD) | Mini-mum | Maxi-mum | Mean ( ± SD) | Mini-mum | Maxi-mum | |
| BUN | | | | | | | |
| Intervention | 63.1 ± 20.8 | 39 | 107 | 63.1 ± 17 | 31 | 99 | > .05 |
| Control | 65.8 ± 22.4 | 35 | 116 | 74.3 ± 24.1 | 40 | 137 | |
| Cr | | | | | | | |
| Intervention | 8 ± 2.4 | 5.6 | 14.8 | 8.2 ± 2.4 | 5.1 | 14 | > .05 |
| Control | 9.6 ± 3.8 | 4.4 | 19 | 10.5 ± 4.3 | 6.5 | 20.7 | |
| Na | | | | | | | |
| Intervention | 138.6 ± 4.4 | 132 | 148 | 140 ± 2.7 | 134 | 145 | > .05 |
| Control | 137.8 ± 2.6 | 133 | 143 | 140.5 ± 3 | 136 | 147 | |
| K | | | | | | | |
| Intervention | 5.3 ± 0.6 | 4.4 | 6.3 | 5.5 ± 0.6 | 4.6 | 7 | > .05 |
| Control | 5.1 ± 0.7 | 4 | 6.9 | 5.8 ± 1 | 3.6 | 7.5 | |
| Hb | | | | | | | |
| Intervention | 9.8 ± 1.1 | 7.6 | 11 | 12 ± 1.4 | 9.8 | 14.8 | > .05 |
| Control | 10.2 ± 1 | 8.1 | 11 | 11.5 ± 1.2 | 9.2 | 13.7 | |
| Plt | | | | | | | |
| Intervention | 197.4 ± 79.2 | 82 | 400 | 192.1 ± 71.8 | 117 | 400 | > .05 |
| Control | 193.2 ± 84.4 | 138 | 490 | 177.2 ± 53 | 117 | 339 | |

dL), Cr (mg/dL), Na (mmol/L), K (mmol/L), Hb (g/dL), and Plt count (*$10^3$) at the beginning and end of the study. The patients did not significantly differ in the levels of urea, sodium, and potassium before and after the study ($P > .05$).

The control patients who received placebo along with erythropoietin showed increased levels of total ferritin and serum iron during the study, but those patients receiving vitamin C along with erythropoietin showed decreased levels of ferritin.. The mean iron level increased in both intervention and control groups. Also, TIBC level was found to be higher in patients under intervention, and lower in the control patients.

All the patients demonstrated an increasing trend in the mean TSAT from the beginning to the end of the study. Values of these laboratory parameters have been listed in Tables 3 and 4. In this study, the effect of vitamin C injection on reducing ferritin levels was significant ($P < .05$); but no correlation was found between vitamin C injection and other lab parameters (Tables 3 and 4).

The frequency and duration of hemodialysis before the study did not differ between the two groups ($P > .05$). Using the Mann-Whitney test, at the end of the study, the number of hemodialyses and its duration did not differ significantly between the patients who received vitamin C and those who received placebo.

Chi-square statistical test was used to compare between levels of C-reactive protein (CRP) in the two groups. The intervention patients and the controls did not show a significant difference in the mean CRP levels ($P > .05$); thus, CRP level was not a confounding factor. Nevertheless, CRP levels were also assessed at the end of the third month, and the mean levels did not differ significantly from CRP levels at the beginning of the study.

In the present study, the length of hemodialysis (hours per session), the number of weekly hemodialysis sessions, and the dialysis adequacy index were also evaluated. To investigate the factors affecting dialysis adequacy in the study, the variables which potentially could affect dialysis at the end of the study were entered into a logistic regression model.

These potential variables affecting dialysis adequacy at the end of the study were almost equal to those affecting dialysis adequacy at the beginning of the study ($P = .032$, Odds Ratio = 5.714). Also, the participants who had adequate dialysis before the intervention had a 5.71-fold increased chance of adequate dialysis at the end of the study compared with those who did not have adequate dialysis. Other variables including the type of intervention (either vitamin C or placebo) had no significant effects on dialysis adequacy at the end of the study.

## DISCUSSION

Patients undergoing hemodialysis are at risk of anemia due to decreased production of red blood cells in the bone marrow and their increased loss due to hemolysis. Iron supplements are one of the treatments for anemia in these patients,

**Table 3.** Mean Ferritin (ng/mL), Iron (mcg/dL), TIBC (g/dL), Transferrin Saturation (%) in patients Undergoing Hemodialysis at the Beginning and the End of the Study

| | Intervention | | | | Control | | | |
|---|---|---|---|---|---|---|---|---|
| | Fe | Iron | TIBC | T Sat% | Fe | Iron | TIBC | T Sat% |
| Mean | 855 | 53 | 280 | 18 | 1044 | 62 | 323 | 19 |
| Standard Deviation ( ± SD) | 223 | 29.6 | 145.8 | 1 | 654.6 | 13.6 | 67.8 | 0.7 |
| Minimum | 504 | 25 | 130 | 15.2 | 515 | 43 | 224 | 16 |
| Maximum | 1282 | 146 | 735 | 19 | 3231 | 99 | 498 | 19 |

**Table 4.** Mean Ferritin (ng/mL), Iron (mcg/dL), TIBC (g/dL), Transferrin Saturation (%) in Renal Failure Patients Undergoing Hemodialysis at the End of the Study

| | Intervention | | | | Control | | | |
|---|---|---|---|---|---|---|---|---|
| | Fe | Iron | TIBC | T Sat% | Fe | Iron | TIBC | T Sat% |
| Mean | 565 | 75 | 306 | 22 | 1453 | 71 | 308 | 23 |
| Standard deviation ( ± SD) | 181.8 | 89.9 | 257.6 | 7.8 | 827.1 | 17.8 | 56.8 | 3.8 |
| Minimum | 323 | 19 | 120 | 14 | 551 | 44 | 220 | 18 |
| Maximum | 950 | 403 | 1238 | 44.6 | 3950 | 115 | 449 | 29 |

which are associated with increased iron load in the body and serum ferritin levels. Furthermore, vitamin C is a low-risk dietary supplement and has been recommended to reduce the need for iron supplements and ferritin levels in patients with renal insufficiency.

In this study, we reviewed the results of a three-month use of intravenous ascorbic acid in a triple-blind clinical trial. In this regard, we evaluated two groups of hemodialysis patients (intervention and control) to assess the changes in ferritin levels before and after receiving intravenous ascorbic acid. Additionally, the amount of laboratory parameters such as BUN, creatinine, sodium, potassium, hemoglobin, platelets count, ferritin, serum iron, TIBC, transferrin saturation, and CRP were evaluated at the beginning and end of the three months of study. The results of our study showed that there was a significant relationship between vitamin C intake and serum ferritin level. In patients who received vitamin C injection, the average ferritin level was found to be reduced at the end of the study. Therefore, intravenous vitamin C can be used as an adjunct in the treatment of anemia in hemodialysis patients. In the current study, there were no significant differences between the levels of hemoglobin, platelets, creatinine, and transferrin saturation between the two groups.

In 2012, Kang *et al.* conducted a study on the effect of intravenous ascorbic acid in hemodialysis patients with normal levels of ferritin (between 100 and 500 micrograms per liter).[14] In the intervention group, the patients received 500 mg of intravenous ascorbic acid with each dialysis session for three months. Following this, the patients were followed for 4 months. They showed that 20 patients in the intervention group, had a significant increase in hemoglobin level (Hb increase > 1 g/dL) and a decrease in the weekly dose of erythropoietin, compared with the control group after 3 months of treatment ($P < .05$). Therefore, intravenous ascorbic acid administration can be a strong and effective adjunct therapy for patients undergoing hemodialysis with erythropoietin-resistant anemia. In addition, ascorbic acid can reduce the dose of erythropoietin needed to correct anemia. Shinawi *et al.* have stated that intravenous ascorbic acid, as an adjunct therapy with an iron supplement, has a significant effect on serum Hb, serum ferritin, and CRP in patients with End-Stage Renal Disease.[15] Also, a low daily dose of vitamin C oral supplement can reduce the need for a dose of erythropoietin in hemodialysis patients with functional IDA.[16] These findings confirm the results of our study. On the contrary, in a study of 39 hemodialysis patients, Bashardoost *et al.* stated that serum iron, TIBC, and transferrin saturation were not significantly different from in the group treated with vitamin C compare with the control group. Therefore, they claimed that vitamin C did not affect serum ferritin, iron, and transferrin saturation.[17]

Recent clinical studies have shown that hyperuricemia occurs in patients undergoing hemodialysis with complications such as cardiovascular mortality and inadequate dialysis. Biniaz *et al.* examined the effect of vitamin C supplements on serum uric acid levels in hemodialysis patients and stated that there was a significant negative relationship between vitamin C and serum uric acid levels, but the mean serum creatinine levels did not change significantly during the study. [(18)] Our study also showed that vitamin C intake did not affect BUN level and serum creatinine during the hemodialysis sessions.

Significant platelet activation can occur during hemodialysis and platelet surface markers show evidence of platelet degranulation. The platelet count decreased slightly in the first hour of dialysis, but in most cases, it returned to baseline by the end of dialysis. Several cases of chronic hemodialysis patients have been reported in which a significant reduction in platelet count (50% or more) was observed during dialysis, leading to mild degrees of thrombocytopenia.[19,20] Our results showed that during the course of this study, the overall mean platelet count in both intervention and control groups decreased during dialysis, and vitamin C intake had no effect on serum platelet levels. Also, low doses and short-term use of vitamin C are ineffective procedures.[21]

Chronic inflammation is the most important cause of cardiovascular disease in patients undergoing hemodialysis; In such patients, ascorbic acid can be effective as a major antioxidant in reducing inflammation.[22] Although the available data on the effect of vitamin C on CRP levels in hemodialysis patients is inconsistent, studies have shown that there is an inverse relationship between serum levels of vitamin C and CRP. In the present study, vitamin C intake had no effect on CRP levels and no significant difference in CRP levels was observed between the placebo and intervention groups. These results were inconsistent with the results of Biniaz *et al.* who showed a decreased level of CRP level in the intervention group receiving vitamin C supplementation compared with the control group.[18,23]

Our study showed that the only variable that significantly affected dialysis adequacy at the end of our study was the value of dialysis adequacy at the beginning of the study. Other variables including the study intervention had no significant effect on dialysis adequacy at the end of the study. Our study also showed that vitamin C intake does not affect serum sodium and potassium levels, the number of weekly sessions, and the duration of each hemodialysis session.

One of the limitations of this study is the small sample size; Hence, we recommend subsequent studies be conducted with larger sample size and a longer study duration, to efficiently examine the role of vitamin C in reducing serum ferritin levels. Also, considering the prevalence of anemia in non-hemodialysis patients of other diseases, it is recommended to evaluate the possible side-effects and benefits of ascorbic acid in such patients.

## CONCLUSION

The results of the current study showed that injection of vitamin C could reduce serum ferritin levels in hemodialysis patients. Therefore, intravenous vitamin C can be used as an adjunct in the treatment of anemia in these patients, as a cheap and available therapy, with few known complications in hemodialysis patients.

## REFERENCES

1. National Institute of Diabetes and Digestive and Kidney Diseases. June 2017. Retrieved 19 December 2017.
2. Murdeshwar HN, Anjum F. Hemodialysis. [Updated 2020 Dec 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK563296/.
3. Lee K-H, Ho Y, Tarng D-C. Iron Therapy in Chronic Kidney Disease: Days of Future Past. International Journal of Molecular Sciences. 2021;22(3):1008.
4. Babitt JL, Lin HY. Mechanisms of anemia in CKD. Journal of the American Society of Nephrology. 2012;23(10):1631-4.
5. Park H, Liu X, Henry L, Harman J, Ross EA. Trends in anemia care in non-dialysis-dependent chronic kidney disease (CKD) patients in the United States (2006–2015). BMC nephrology. 2018;19(1):1-10.
6. Yiannikourides A, Latunde-Dada GO. A Short Review of Iron Metabolism and Pathophysiology of Iron Disorders. Medicines (Basel). 2019;6(3):85. Published 2019 Aug 5. doi:10.3390/medicines6030085.
7. VanWagner LB, Green RM. Elevated serum ferritin. JAMA. 2014;312(7):743-4.
8. Knovich MA, Storey JA, Coffman LG, Torti SV, Torti FM. Ferritin for the clinician. Blood reviews. 2009;23(3):95-104.
9. D'Costa MR, Winkler NS, Milliner DS, Norby SM, Hickson LJ, Lieske JC. Oxalosis Associated With High-Dose Vitamin C Ingestion in a Peritoneal Dialysis Patient. American journal of kidney diseases : the official journal of the National Kidney Foundation. 2019;74(3):417-20.
10. Handelman GJ. New insight on vitamin C in patients with chronic kidney disease. Journal of Renal Nutrition. 2011;21(1):110-2.
11. Ogawa T, Nitta K. Erythropoiesis-stimulating agent hyporesponsiveness in end-stage renal disease patients. Chronic Kidney Diseases-Recent Advances in Clinical and Basic Research. 2015;185:76-86.
12. Nand N, Deshmukh A, Mittal R. Evaluation of Effect of Ascorbic Acid on Ferritin and Erythropoietin Resistance in Patients of Chronic Kidney Disease. The Journal of the Association of Physicians of India. 2017;65(7):32-6.
13. Jalalzadeh M, Shekari E, Mirzamohammadi F, Ghadiani M. Effect of short-term intravenous ascorbic acid on reducing ferritin in hemodialysis patients. Indian Journal of Nephrology. 2012;22(3):168.
14. Kang DW, Ahn CY, Ryu BK, Shin BC, Chung JH, Kim HL. The effect of intravenous ascorbic acid in hemodialysis patients with normoferritinemic anemia. Kidney research and clinical practice. 2012;31(1):48-53.
15. El Shinnawy H, Khedr AR, Alghitany A, Ramzy M, Baki AH. Role of intravenous ascorbic acid in the management of anemia in hemodialysis patients. Indian J Nephrol [Epub ahead of print] [cited 2021 Feb 17]. Available from: https://www.indianjnephrol.org/preprintarticle.asp?id = 300209.
16. Sultana T, DeVita MV, Michelis MF. Oral vitamin C supplementation reduces erythropoietin requirement in hemodialysis patients with functional iron deficiency. International urology and nephrology. 2016;48(9):1519-24.
17. Bashardoust B, Zakeri A, Jastan M, Amani F, Habibzadeh A, Khatami F. Impact of vitamin C supplementation on serum ferritin level in hemodialysis patients. Journal of Nephropathology. 2018;7(3):197-200.
18. Biniaz V, Shermeh MS, Ebadi A, Tayebi A, Einollahi B. Effect of vitamin C supplementation on C-reactive protein levels in patients undergoing hemodialysis: A randomized, double blind, placebo-controlled study. Nephro-urology monthly. 2014;6(1).
19. Daugirdas JT, Bernardo AA. Hemodialysis effect on platelet count and function and hemodialysis-associated thrombocytopenia. Kidney international. 2012;82(2):147-57.
20. Mohammed BM, Sanford KW, Fisher BJ, Martin EJ, Contaifer Jr D, Warncke UO, et al. Impact of high dose vitamin C on platelet function. World journal of critical care medicine. 2017;6(1):37.

21. Farsi Z. Effect of stress oxidative on kidney disease. J Baqiyatallah Univ Med Sci. 2008;27:22-3.
22. Kubota Y, Moriyama Y, Yamagishi K, Tanigawa T, Noda H, Yokota K, et al. Serum vitamin C concentration and hs-CRP level in middle-aged Japanese men and women. Atherosclerosis. 2010;208(2):496-500.
23. Biniaz V, Tayebi A, Ebadi A, Shermeh MS, Einollahi B. Effect of vitamin C supplementation on serum uric acid in patients undergoing hemodialysis: a randomized controlled trial. Iranian journal of kidney diseases. 2014;8(5):401.

Correspondence to:
Mohhamad Taheri, MD
Velayat Hospital, Taavon Square, 22 Bahman Blvd, Elahieh, PO Box: 3471976161, Qazvin, Iran
Tel: 0098 2833 790 611
Fax: 0098 2833 790 611
E-mail: mohammaadtaheri@yandex.com

Received August 2021
Revised October 2021
Accepted December 2021