
Long-term Complications of Hemodialysis

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Abstract:

Hemodialysis is one of the renal replacement therapies, besides peritoneal dialysis and renal transplantation. Although hemodialysis can improve morbidity and mortality in renal patients, it has many complications that occur during the dialysis sessions and/or as long term use of hemodialysis.

Hypotension, hypoglycemia, electrolyte disturbances, disequilibrium syndrome, hypocalcaemia etc are common complications occur during dialysis. In long-term dialysis, there are complications as amyloidosis, bone disease, endocrine disturbances, infection, cardiovascular complications, vascular access and nutrition complication. Important long-term hemodialysis complications will be reviewed in this article.

Key words. Hemodialysis, hypotension, muscle cramps, infection transmission, Amyloidosis, HD complications

Introduction:

Renal replacement therapy is an option to treat patients with acute and/or chronic renal failure. There are two treatment options for a patient who develops end stage renal failure with evidence of uremia symptoms. Kidney transplantation is the best option in treating end-stage renal failure (ESRF) patients, however, shortage of donated-organs, pre and post transplantation follow up and worldwide transplantation team availability are obstacles and difficulties in many countries. These reasons have led to the other alternatives of renal replacement therapy modality which is dialysis particularly hemodialysis.

The underlying cause of end-stage renal disease (ESRD) is increasingly changing. In the United States, about 40% of patients have ESRD due to diabetes, hypertension, recurrent urinary tract infection, drug use, glomerulopathies, vasculitic diseases etc. The average age of patients commencing dialysis has risen to 64 years. This increase in starting dialysis age has led to more co-existent diseases that associated with aging as well dialysis complications.¹

The commonly used modality of renal replacement is hemodialysis (HD). HD for ESRD started in human in 1960 with development of the Teflon arteriovenous shunt by Scribner and co-workers at the University

of Washington. The number of patients increased steadily, up to year 2002 about 250.000 in the United State and more than 500.000 patients worldwide were on dialysis.²

The most frequent long-term complications in HD patients are related to cardiovascular disease, β 2-microglobulin (β 2M) amyloidosis, renal osteodystrophy, vascular access, malnutrition, and infection transmission across HD-dependent patients. These complications will be reviewed.

1. Cardiovascular complications

Cardiovascular disease (CVD) is the major cause of death in ESRD patients on regular HD. Atherosclerosis is present in most if not all long-term dialysis patients. CVD in HD patients is 5 to10 times higher than in general population, and it accounts for at least half of all patients' deaths. The death in these patients were mainly due to coronary heart disease (CHD).³ Diagnosis of CHD in chronic dialysed patients requires coronary artery bypass surgery that has more than three times increase in mortality rate in CKD patients than general population.⁴

Hypertension is not common in HD patients and it is usually difficult to control due to many factors. Poorly controlled hypertension is a major risk factor for CVD.⁵ Other risk

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factors that may increase the chance of CHD are hyper-phosphatemia and elevated calcium-phosphorus product with calcium deposition in the coronary arteries, the cardiac conduction system,⁶⁻⁸ heart valves⁶ and blood vessels elsewhere. Anemia,⁹ hypertriglyceridemia¹⁰ low HDL-cholesterol¹¹ increased lipoprotein,¹² insulin deficiency or resistance,¹³ high homocystein in blood,¹⁴ endothelial dysfunction,¹⁵ inflammation and elevated C-reactive protein,¹⁶ and smoking¹⁷ are common, and they increase the risk of CHD significantly. Many if not all of these risk factors may have been occurred during the years of chronic renal insufficiency before even starting HD. Reducing the CVD complications in ESRD can be achieved by modifying these risk factors.

Hypertension control by drugs is very necessary.^{18,19} Adequate and prolonged HD is recommended, and it should be carried to control hypertension in HD patients.²⁰ Reducing LDL-cholesterol concentration is of great importance to minimize the risk of myocardial cardiac infarction in non-renal and HD patients with coronary heart disease.²¹ Vitamin E has been suggested as a means of reducing oxidative stress and cardiovascular mortality.^{22,23} Achieving lower plasma LDL-cholesterol with Cerivastatin that has also anti-inflammatory effect may reduce long term HD complications in HD-patients.⁸

Hyperphosphatemia and elevated calcium phosphate product, and the use of calcium based phosphate binders are high risk factors for vascular calcification.^{6,9,24} Low calcium dialysate content and selective vitamin D analogues use helps to minimize and improve bone and vascular calcification complications.

Anemia is a commonest complication in HD-patients. It is a major risk factor for CVD and increasing mortality in HD patient. Anemia correction by adequate tonic supplements, erythropoietin and adequate HD patients improves cardiovascular dynamics, exercise tolerance and morbidity as well the mortality.⁴

Cardiac disease in HD dependent ESRD is usually managed with ordinary treatment measures of cardiac problems, however, percutaneous transluminal coronary angioplasty, stenting and bypass surgery are indicated in HD patients. These interventional measures have higher risk mortality, recurrence and restenosis than general population.²⁵

2. Amyloidosis

β_2 M amyloid deposition begins usually during few months of starting HD. The clinical and radiological amyloid findings appear usually after five years or more of HD. Sternoclavicular and hips joint are commonly the first joints involved, however, any joint can be affected. Severe spinal cord compression due to β_2 M amyloidosis deposition occurs often after ten years of HD²⁶. Amyloidosis deposition at the joints may present clinically by features of peri-arthritis of the shoulders, carpal tunnel syndrome, flexor tenosynovitis of the hands, stiffness, pain and swelling of other joints, deposits beneath the skin and spondyloarthropathy.²⁷ After fifteen years of regular HD, β_2 M amyloid systemic infiltration of visceral organs occurs, but it is usually asymptomatic.

β_2 M amyloidosis pathology is not well established and poorly understood. It is reported, following successful renal transplantation, amyloid symptoms improve and its progression halts with reduction in plasma β_2 amyloid.^{28,29} Others have reported that the available HD modalities can remove some of produced β_2 M, but it will not reduce the amount of β_2 M amyloid that can prevent the known amyloidosis complications, even with high- flux dialysis using ultrapure water to produce dialysate.³⁰

3. Osteodystrophy

Long-term HD increases osteodystrophy risk. Osteodystrophy is commonly associated with secondary hyperparathyroidism that is characterized by high plasma parathyroid hormone despite of normal serum calcium and phosphate.³¹

Osteodystrophy prevalence in long-term HD patients, together with impaired handling and buffering of calcium loads that accompany secondary hyperparathyroidism is increasing.³⁷ Hip fractures frequency due to osteodystrophy is more frequent and serious in long-term HD patients than in the matched general population.³² Dynamic and adynamic bone diseases occur in CKD patients, but their prevalence is more after starting HD.

4. Undernutrition

Undernutrition is often common in HD dependent patients, and time duration on dialysis is a strong predictor of malnutrition.³³

Patients on HD more than ten year are tending to loss their body weight despite adequate protein intake.³⁴ Although the underlying cause of malnutrition is unclear, it is may be due to chronic metabolic acidosis, or to decreased physical activity as a result of β_2 M-amyloidosis rather than the reduction in energy expenditure. It had been reported that the survival rate is correlated with serum albumin and prealbumin levels.³⁴ Occurrence of adynamic bone disease also appears to relate to malnutrition, although it is unclear whether this is a causal relationship, or whether both conditions are characteristic of long-term HD survivors.³⁵ Zinc and selenium deficiency have been reported in chronic dialysis patients which is mostly due to malnutrition and reverse osmosis water treatment may has role.³⁶

5. Vascular Access

Vascular access of HD should be planned as early as possible, especially in elderly and diabetic patients. Native arteriovenous fistula (AV) is always recommended whenever possible.³⁷ Early dialysis must be initiated, while it reduces the frequency of complications, but may or may not improve patient survival during the first few months of treatment.^{38,39} Complications of vascular access as infection, malfunction, stenosis, disfigurement etc are major concern, and can lead to inadequate dialysis.

Hemodialysis vascular access infection is common causes for hospitalization in HD patients, and can cause serious complications. In less serious catheter and graft infections, it is sometimes possible to eradicate the infection with several weeks antibiotics course. The persistence of fevers, an elevated number of white blood cells in the blood, or constitutional symptoms, all can indicate antibiotic treatment failure, and that indicates the vascular access should be removed.

AV grafts are less likely to become infected than catheters and non-native fistula. When AV grafts become infected, it is usually due to hematoma formation that spreads to graft material. So, HD patients should avoid prolonged use of hemodialysis catheters, because they are associated with frequent and serious infections. Strict hygienic sterile methods should be applied to reduce the risk of the infection.

6. Infection transmission

Dialysis has led to decrease mortality and morbidity in ESRD patients, but it predisposes these patients to blood born infections, partly due to an abnormal immune system function in CKD patients and in dialysis dependent ESRD patients. In dialysis patients, white blood cells count may be normal, but the white blood cells are typically not functioning normal. This abnormality has led to more risk of staphylococcus infection.

Lymphocytes are primarily involved in protection against infections caused by viruses and fungi. HD dependent patients have increased incidence of viral and fungal infections due to lymphocyte malfunctioning. Simple viral infections as influenza occurs, but also serious conditions such as shingles and hepatitis are not common. Hence, vaccinations against these infections decrease the severity of these viral infections.

The spread of infectious agents from the dialysis machine or other dialysis related procedures to the patient is unusual in the setting of current infection control policies, but it does rarely occur. Dialysate fluid might be contaminated with an infectious agent, and theoretically can transmit infections, although the dialyzer membrane material is an effective barrier to the spread of these agents from the machine to patient's blood. Infection related to the dialysis treatment is unusual, but it can occur during the put-on or take-off process where infectious agents can be introduced into the patient's vascular access due to improper sterile technique. Therefore, it is important for patients to become familiar with and he/she should insist that sterile technique must be used during the beginning and ending of dialysis treatment.

Various studies have shown a higher prevalence of HBV, HCV and HIV in HD patients than in the general population.^{40,41} The increase of these viruses infection may be due to dialysis machines sharing, inappropriate preparation of parenteral drugs and inadequate infection control methods in dialysis units. Blood transfusion needs and the suppressed immunity of patients may also have role in these viruses' transmission.⁴²

HCV infected patients are usually asymptomatic. This is leading to higher HCV transmission risk because these patients and

the HD staff was unaware about the infection transmission risk, and this may not made them strictly compliant to the standard infection measures. It has been suggested that HCV transmission in dialysis units is mainly a result of environmental contamination, therefore, currently dedicated machines are not commonly recommended for HCV- positive patients. Furthermore, due to the lack of an effective HCV-vaccine has led to higher risk of chronic HCV hepatitis in HD patients.

A determined average prevalence of HCV in hemodialysis patients in Iran were 13.2%, while others reported lesser prevalence in other areas of Iran.⁴³ Alavian et al⁴⁴ (2012) reported, the average rate of HCV infection in HD patients in 12 areas in Iran has been estimated about 7.6%, and it has been concluded that Iran is among the low-prevalence countries in terms of HCV in hemodialysis patients.⁴⁵

Prevalence of hepatitis virus infections seems to be higher in underdeveloped and developing countries than in developed countries. The prevalence of HBV and HCV in Palestine has been reported to be 8.1% and 22% respectively.⁴⁶ In Yemen, the HCV prevalence rate was 62.7%.⁴⁷ In the Middle East, the rate of HCV infection in HD patients is higher; in Jordan, Syria (28%, 48% respectively).^{48,49} High incidence of HCV has been noted in some countries as India where 83% prevalence is reported in dialysis patients,⁵⁰ 71% prevalence reported in Venezuela⁵¹ and 46% in Saudi Arabia.⁵² A low prevalence of 5.72% was noted in Switzerland,⁵³ while in France it was 7.7%.⁵⁴ These differences might be due to the time period elapsed on hemodialysis, dialysis machine availability and good strict compliant of staff and patients to infection control rules.

HBV infection was also found in 7% of HD patients in the Kerman Province which is similar to other studies in other areas of the country. In the Khuzestan Province, 5.1%,⁵⁷ and in Uromiye 6.5%⁵⁶ of the hemodialysis patients had positive HBs-Ag. The prevalence of positive HBs-Ag in the general population of Iran has been estimated to be 2.6%.⁵⁸ These findings also support the higher prevalence of HBV in HD patients. The role of occult

hepatitis B infection in the spread of infection may need more attention. Despite negative HBs-Ag, these patients may have positive HBV- DNA and may infect others.

Prevention of CKD and its late consequences should be the ultimate goal of health-care providers. In order to improve the survival and reduce the morbidity in all CKD patients, it is essential to optimize the pre-ESRD care of patients with chronic renal insufficiency. It is documented that strict blood pressure control with ACE-inhibitors, ARBs or other hypertensive medical therapy,⁵⁹ protein restriction,⁶⁰ tight control of diabetes,^{61,62} anemia correction by improving nutrition and erythropoietin⁶³ can reduce or may delay the need for dialysis. Lipid profile control is also an important issue to prevent complications - especially the cardiovascular complications- that may occur in CKD patients either pre-during or- after HD.⁶⁴ Moreover, Focus on the prevalence of HBV, HCV hepatitis and HIV in HD centers and the determination of their risk factors helps health planners to establish more effective measures to reduce their prevalence and recirculation, mortality and ultimately reduce rates of morbidity.⁶⁵ These tasks can be achieved by strict adherence to infection control measures - routine screening of donated blood products, separation of HBV, HCV and HIV dedicated dialysis machines, HBV vaccination and periodic testing for HBV, HVC and HIV infection markers. Patients' compliance and staff to follow national and international recommendations must be strictly applied.

7. Conclusion:

Considering the varied factors that may affect the morbidity and mortality of HD patients and the steady increase in patients with CKD on HD worldwide, it is clear that there is a huge need for more research to assign the best way to diagnose and to treat kidney diseases at early stages to prevent late complications of CKD and HD. Further collaborative national and international multicenter outcome researches are needed to establish the preventive and treatment guide lines that can be helpful and positively affect morbidity and mortality in kidney diseases and the long-term complications of dialysis.

8. References:

1. Locatelli F, Manzoni C, Del Vecchio L, Di Filippo S. Changes in the clinical condition

of haemodialysis patients. *J Nephrol* 1999; 12(Suppl 2):82-91

2. Blagg R C. Long-term Complications in Hemodialysis. *SJKDT* 2001; 12: 487-493.
3. Levey AS, Beto JA, Coronado BE, Eknayan G, Foley RN, Kasiske BL, Klag MJ, Mailloux LU. Controlling the epidemic of cardiovascular disease in chronic renal disease: What do we know? What do we need to learn? Where do we go from here? *Am J Kidney Dis* 1998;32:853-906.
4. Liu JY, Birkmeyer NJ, Sanders JH, Morton JR, Henriques HF, Lahey SJ, Dow RW. Risks of morbidity and mortality in dialysis patients undergoing coronary artery bypass surgery. Northern New England Cardiovascular Disease Study Group. *Circulation* 2000;102:2973-7.
5. Foley RN, Parfrey PS, Harnett JD, Kent GM, Murray DC, Barre PE. Impact of hypertension on cardiomyopathy, morbidity and mortality in end-stage renal disease. *Kidney Int* 1996;49:1379-85.
6. Raggi P. Detection and quantification of cardiovascular calcifications with electron beam tomography to estimate risk in hemodialysis patients. *Clin Nephrol* 2000;54: 325-33.
7. Goodman WG, Goldin J, Kuizon BD, Yoon C, Gales B, Sider D, Wang Y, Chung J, Emerik A, Greaser L, Elashoff RM, Salusky BI. Coronary artery calcification in young adults with end-stage renal disease who are undergoing dialysis. *N Engl J Med* 2000;342:1478-83.
8. Isotalo PA, Halil A, Green M, Tang A, Lach B, Veinot JP. Metastatic calcification of the cardiac conduction system with heart block: an under-reported entity in chronic renal failure patients. *J Forensic Sci* 2000; 45:1335-8).
9. Mocks J. Cardiovascular mortality in hemodialysis patients treated with epoetin beta-a retrospective study. *Nephron* 2000; 86:455-62.
10. Oda H, Keane WF. Lipid abnormalities in end stage renal disease. *Nephrol Dial Transplant* 1998;13(Suppl 1):45-9.
11. Gordon DJ, Probstfield JL, Garrison RJ, Neaton JD, Castelli WP, Knoke JD, Jacobs DR Jr, Bangdiwala S, Tyroler HA. High-density lipoprotein cholesterol and cardiovascular disease. Four prospective American studies. *Circulation* 1989;79:8-15.
12. Kronenberg F, Utermann G, Dieplinger H. Lipoprotein(a) in renal disease. *Am J Kidney Dis* 1996;27:1-25.
13. Attman PO, Samuelsson O, Alaupovic P. Lipoprotein metabolism and renal failure. *Am J Kidney Dis* 1993;21:573-92.
14. Van Guldener C, Robinson K. Homocysteine and renal disease. *Semin Thromb Hemost* 2000;26:313-24.
15. Ross R. Atherosclerosis: an inflammatory disease. *N Engl J Med* 1999;340:115-26.
16. Arici M, Walls J. End-stage renal disease, atherosclerosis, and cardiovascular mortality: Is C-reactive protein the missing link? *Kidney Int* 2001;59:407-14.
17. Orth S, Ogata H, Ritz E. Smoking and the kidney. *Nephrol Dial Transplant* 2000;15: 1509-11.
18. Scribner BH. Can antihypertensive medication control BP in hemodialysis patients: yes or no? *Nephrol Dial Transplant* 1999; 14:2599-601.
19. Charra B, Bergstrom J, Scribner BH. Blood pressure control in the dialysis patients: importance of the lag phenomenon. *Am J Kidney Dis* 1998;32: 720-4.
20. Charra B, Caemard M, Laurent G. Importance of treatment time and blood pressure control in achieving long-term survival on dialysis. *Am J Nephrol* 1996;16:35-44.
21. Baigent C, Wheeler D. Should we reduce blood cholesterol to prevent cardiovascular disease among patients with chronic renal failure? *Nephrol Dial Transplant* 2000;15: 1118-9.
22. Boaz M, Smetana S, Weinstein T, Matas Z, Gaftor U, Iaina A, Knecht A, Weissgarten Y, Brunner D, Fainaru M, Green MS: Secondary prevention with antioxidants of cardiovascular disease in endstage renal disease (SPACE): randomised placebo-controlled trial. *Lancet* 2000, 356:1213-1218.
23. Mune M, Yukawa S, Kishino M, et al. Effect of vitamin E on lipid metabolism and atherosclerosis in ESRD patients. *Kidney Int Suppl* 1999;71:126-9.
24. Vaitkus P. Current status of prevention, diagnosis, and management of coronary artery disease in patients with kidney failure. *Am Heart J* 2000;139:1000-8.
25. Kay J, Bardin T. Osteoarticular disorders of renal origin: disease-related and iatrogenic. *Baillieres Best Pract Res Clin Rheumatol* 2000;14:285-305.
26. Floege J, Ketteler M. Beta2-microglobulin-derived amyloidosis: an update. *Kidney Int* 2001;59(Suppl 78):S164-71.

27. Bardin T; Lebail-Darné JL; Zingraff J; Laredo JD; Voisin MC; Kreis H; Kuntz D. Dialysis arthropathy: outcome after renal transplantation. *Am J Med* 1995;99:243-8.
28. Locatelli F, Mastrangelo F, Redaelli B, Ronco C, Marcelli D, Orlandini Gand the Italian Cooperative Dialysis Study Group. Effects of different membranes and dialysis technologies on patient treatment tolerance and nutritional parameters. *Kidney Int* 1996;50:1293-302.
29. Chertow GM, Plone M, Dillon MA, Burke SK, Slatapolsky E. Hyperparathyroidism and dialysis vintage. *Clin Nephrol* 2000;54:295-300.
30. Cannata JB. Adynamic bone and chronic renal failure: An overview. *Am J Med Sci* 2000;320:81-4.
31. Coco M, Rush H. Increased incidence of hip fractures in dialysis patients with low serum parathyroid hormone. *Am J Kidney Dis* 2000;36:1115-21.
32. Marcen R, Teruel JL, de la Cal MA, Gamez C. Spanish Cooperative Study of Nutrition in Hemodialysis. The impact of malnutrition in morbidity and mortality in stable haemodialysis patients. *Nephrol Dial Transplant* 1997;12:2324-31.
33. Combe C, Chauveau P, Laville M, Fouque D, Azar R, Cano N, Canaud B, Roth H, Leverve A. Influence of nutritional factors and hemodialysis adequacy on the survival of 1,610 French patients. *Am J Kidney Dis* 2001;37(Suppl 2):81-8.
34. Fukagawa M, Akizawa T, Kurokawa K. Is aplastic osteodystrophy a disease of malnutrition? *Current Opin Nephrol Hypertens* 2000; 9:363-7.
35. Zima T, Tesakov M, Mestek O, Nalimelek K. Trace elements in end-stage renal disease: Clinical implications of trace elements. *Blood Purif* 1999;17:187-98.
36. NKF-DOQI. Clinical practice guidelines for vascular access. New York. National Kidney Foundation 1997:69.
37. Ellis PA, Reddy V, Bari N, Cairns HS. Late referral of end-stage renal failure. *QJM* 1998; 91:727-32.
38. Roubicek C, Brunet P, Huiart L, Thirion X, Leonetti F, Dussol B, Jaber K, Andrieu D, Ramanarivo P, Berland Y. Timing of nephrology referral: influence on mortality and morbidity. *Am J Kidney Dis* 36: 35-41, 2000
39. Woods JD, Port FK, Orzol S, Buoncristiani U, Young E, Wolfe RA, Held PJ. Clinical and biochemical correlates of starting "daily" hemodialysis. *Kidney Int* 1999; 55: 2467-76.
40. Zahedi MJ, Darvish Moghadam S, Alavian SM, Dalili M. Seroprevalence of hepatitis viruses B, C, D and HIV infection among hemodialysis patients in kerman province, South-East Iran. *Hepat Mon.* 2012;12(5):339-42
41. Elamin S, Abu-Aisha H. Prevention of hepatitis B virus and hepatitis C virus transmission in hemodialysis centers: review of current international recommendations. *Arab J Nephrol Transplant.* 2011;4(1):35-47.
42. Alavian SM, Einollahi B, Hajarizadeh B, Bakhtiari S, Nafar M, Ahrabi S. Prevalence of hepatitis C virus infection and related risk factors among Iranian haemodialysis patients. *Nephrology (Carlton).* 2003;8(5):256-06.
43. Assarehzadegan MA, Shakerinejad G, Noroozkohnejad R, Amini A, Rahim Rezaee SA. Prevalence of hepatitis C and B infection and HC V genotypes among hemodialysis patients in Khuzestan province, southwest Iran. *Saudi J Kidney Dis Transpl.* 2009;20(4):681-4.
44. Alavian SM, Kabir A, Ahmadi AB, Lankarani KB, Shabbabaie MA, Ahmadzad-Asl M. Hepatitis C infection in hemodialysis patients in Iran: a systematic review. *Hemodial Int.* 2010;14(3):253-62.
45. Kafi-abad SA, Rezvan H, Abolghasemi H, Talebian A. Prevalence and trends of human immunodeficiency virus, hepatitis B virus, and hepatitis C virus among blood donors in Iran, 2004 through 2007. *Transfusion.* 2009;49(10):2214-20.
46. El-kader YE-OA, Elmanama AA, Ayesh BM. Prevalence and risk factors of hepatitis B and C viruses among haemodialysis patients in Gaza strip, Palestine. *Virol J.* 2010;7:210.
47. Selm SB. Prevalence of hepatitis C virus infection among hemo- dialysis patients in a single center in Yemen. *Saudi J Kidney Dis Transpl.* 2010;21(6):1165-8.
48. Al-Jamal M, Al-Qudah A, Al-Shishi KF, Al-Sarayreh A, Al-Quraan L. Hepatitis C virus (HCV) infection in hemodialysis patients in the south of Jordan. *Saudi J Kidney Dis Transpl.* 2009;20(3):488-92.
49. Othman B, Monem F. Prevalence of antibodies to hepatitis C virus among hemodialysis patients in Damascus, Syria. *Infection.* 2001;29(5):262-5.

50. Khaja M, Hussain M, Farees N, Krishnan S, Habibullah C. Hepatitis B and C virus infection in chronic renal failure (CRF) patients. *J Gastroenterol Hepatol* 2002; 17(suppl): A 360.).
51. Pujol FH, Ponce JG, Lema MG, Capriles F, Devesa M, Sirit F. High incidence of hepatitis C virus infection in hemodialysis patients in units with high prevalence. *J Clin Microbiol* 1996;34:1633-6.
52. Kashem A, nusairat I, Mohammad M, Ramzy M, Nemma J, Karim MR, Divakaran MP, Tayaab AS. Hepatitis C virus among hemodialysis patients in Najran: prevalence is more among multicenter visitors. *Saudi J Kidney Dis Transplant* 2003;14:206-11.
53. Ambuhl PM, Binswanger U, Renner EL. Epidemiology of chronic hepatitis B and C among dialysis patients in Switzerland. *Schweiz Med Wochenscher* 2000; 130: 341-8.
54. Saune K, Kamar N, Miedouge M, Weclawiak H, Dubois M, Izopet J, Dubois M, Izopet J, Rostaing L. Decreased prevalence and incidence of HCV markers in haemodialysis units: a multicentric French survey. *Nephrol Dial Transplant*. 2011;26(7):2309-16.
55. Gul A, Iqbal F. Prevalence of hepatitis C in patients on maintenance hemodialysis. *J Coll Physician Surg Pak* 2003; 13: 15-8.
56. Khameneh ZR, Sepehrvand N. Survey of hepatitis B status in hemodialysis patients in a training hospital in Urmia, Iran. *Saudi J Kidney Dis Transpl*. 2008;19(3):466-9.
57. Merat S, Rezvan H, Nouraie M, Jamali A, Assari S, Abolghasemi H, Radmard AR, Zaer-Rezaei H, Zeid-Abadi-Nejhad M, Hosseini MR, Amini-Kafiabad S, Maghsudlu M, Pourshams A, Malekzadeh R. The prevalence of hepatitis B surface antigen and anti hepatitis B core antibody in Iran: a population-based study. *Arch Iran Med*. 2009;12(3):225-31
58. Aghakhani A, Banifazl M, Kalantar E, Eslamifar A, Ahmadi F, Razeghi E, Atabak S, Amini M, Khadem-Sadegh A, Ramezani A. Occult hepatitis B virus infection in hemodialysis patients with isolated hepatitis B core antibody: a multicenter study. *Ther Apher Dial*. 2010; 14(3):349–53.
59. Giatras I, Lau J, Levey AS. Effect of angiotensin-converting-enzyme inhibitors on the progression of nondiabetic renal disease: a meta-analysis of randomized trials. *Ann Intern Med* 1997;127:337-45.
60. Tonelli M, Bohm C, Pandeya S, Gill J, Levin A, Kiberd BA. Cardiac risk factors and the use of cardio-protective medications in patients with chronic renal insufficiency. *Am J Kidney Dis* 2001;37:484-9.
61. Pedrini MT, Levey AS, Lau J, Chalmers TC, Wang PH. The effect of dietary protein restriction on the progression of diabetic and nondiabetic renal diseases: a metaanalysis. *Ann Intern Med* 1996;124:627-32.
62. Trocha AK, Schmidtke C, Didjurgeit U, Mühlhauser I, Bender R, Berger M. Effects of intensified antihypertensive treatment in diabetic nephropathy: mortality and morbidity results of a prospective controlled 10-year study. *J Hypertens*. 1999;17:1497-503.
63. Fink J, Blahut S, Reddy M, Light P. Use of erythropoietin before the initiation of dialysis and its impact on mortality. *Am J Kidney Dis* 2001;37:348-55.
64. Hebert LA, Wilmer WA, Falkenhain ME, Ladson-Wofford SE, Nahman NS Jr, Rovin BH. Renoprotection: One or many therapies? *Kidney Int* 2001;59:1211-26.
65. Zahedi MJ, Darvish Moghadam S, Alavian SM, Dalili M. Seroprevalence of hepatitis viruses B, C, D and HIV infection among hemodialysis patients in kerman province, South-East Iran. *HepatMon*. 2012;12(5):339-42.