e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(2); 1132-1141

Original Research Article

A Retrospective Assessment of Mortality and Low Serum Bicarbonate Level in Patients on Hemodiafiltration versus Peritoneal Dialysis: A Comparative Study

Shashank Shekhar[1], Preeti Sinha[2]

[1]Senior Resident, Department of Nephrology, Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, Bihar, India

[2]Junior Resident, Department of Anaesthesia, Sri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, India

Received: 21-12-2022 / Revised: 20-01-2023 / Accepted: 05-02-2023

Corresponding author: Dr Preeti Sinha

Conflict of interest: Nil

Abstract

Aim: In this study, we observed the mortality rate in relation to risk factors including low serum bicarbonate level, coronary artery disease (CAD), and dialysis modality in patients on dialysis during a median follow‑up time of 60 months.

Methods: This was a retrospective study of a cohort of 100 dialysis patients which was conducted at Department of Nephrology, Indira Gandhi institute of Medical Sciences (IGIMS), Patna, Bihar, India for the period of 1 year.

Results: We studied 100 dialysis patients, 66 males and 34 females, on mean age 62.1 ± 14.27 years old. The treatment modalities which were applied were predilution hemodiafiltration (HDF, n = 80), and peritoneal dialysis (PD, n = 20). 80% were with Hemodiafiltration/peritoneal dialysis, 40 5 were having hypertension, 30% were having CAD. We observed that the patients with CAD had higher age, beta2M, i‑PTH, c‑f PWV, PP, AIx, ox‑LDL, and hsCRP but lower serum bicarbonate concentrations, BMI, and albumin than the patients without manifested CAD. We noted that the patients on HDF had lower i‑PTH, serum bicarbonate levels, hsCRP, IR defined by HOMA‑IR but higher albumin, ox‑LDL, and beta2M than the patients on PD. We observed that the patients with serum bicarbonate levels <22 mEq/L were older, they had higher beta2M, HOMA‑IR, i‑PTH, hsCRP, ox‑LDL, c‑f PWV, PP, and AIx, but lower albumin level and lower urine volume in comparison to the patients with serum bicarbonate levels >22 mEq/L.

Conclusion: Uncorrected metabolic acidosis and CAD were shown as independent significant predictors for mortality in patients on renal replacement therapy. PD may provide worse survival after 2–2.5 years of treatment initiation than HDF.

Keywords: Coronary Artery Disease, Hemodiafiltration, Metabolic Acidosis, Peritoneal Dialysis, Survival.

Introduction

A low serum bicarbonate concentration, manifested as an important clinical disturbance of metabolic acidosis, is common in end-stage renal disease (ESRD) and is believed to be an important cause of many deleterious metabolic consequences including protein-energy wasting, inflammation, bone disease, and disturbance in endocrine function. [1-5] The unfavorable effects of metabolic acidosis can explain the increased mortality in patients undergoing maintenance hemodialysis (HD), but the underlying mechanisms are still in need of clarification. In addition, the optimal bicarbonate level to avoid adverse clinical outcomes is largely unknown. [6-9] Along with HD, peritoneal dialysis (PD) is an established treatment modality in ESRD and approximately 150,000 patients worldwide are being maintained on PD. [10] Given the continuous provision of dialysis treatment with PD, it can be presumed that PD may be more effective in correcting metabolic acidosis than HD; thus, the effect of metabolic acidosis on clinical outcomes may differ between the two dialysis modalities.

Dialysis mortality was shown as an eight‐fold higher age‐standardized mortality compared to general population unseparated to dialysis modality. [11] However, it has been reported that mortality may differ between dialysis modality. Comparative studies between patients treated with peritoneal dialysis (PD) and hemodialysis (HD) have frequently shown conflicting results. [12] It has been shown that PD patients have a higher survival rate depended on dialysis vintage for younger and nondiabetic patients than HD patients despite in some studies, HD displayed better survival. [13] Controversially, previous study from a single Chinese center showed that dialysis modality itself has no effect on the survival rate of dialysis patients. [14]

The cardiovascular disease is recognized as the main reason for the increased mortality in dialysis patients. [15] Recently, it has been suggested that the unfavorable effects of metabolic acidosis including malnutrition, inflammation, and oxidative stress can contribute to elevated mortality in dialysis patients. [2,16]

In this study, we observed the mortality rate in relation to risk factors including low serum bicarbonate level, coronary artery disease (CAD), and dialysis modality in patients on dialysis during a median follow‐up time of 60 months.

Materials and Methods

This was a retrospective study of a cohort of 100 dialysis patients which was conducted at Department of Nephrology, Indira Gandhi institute of medical Sciences (IGIMS), Patna, Bihar, India for the period of 1 year

The treatment modalities which were applied were online predilution hemodiafiltration (HDF, n = 80) and PD (n = 20). The median time on HD was 5.0 ± interquartile range 3–10 years and the mean time on PD was 2.8 ± 1.61 years before the starting of our study. In our data, 15 patients were initiated dialysis treatment after the starting of this study, and 85 patients were already in permanent dialysis therapy.

We excluded patients <18 years of age at initiation of dialysis and patients who had <6 months of follow‐up. Patients without regular vascular HD access and who had dialysis catheter and those with autoimmune diseases, infections, or malignancy were excluded from our study. Particularly for the enrolled patients on PD, those who had been on HD or received a kidney transplant before the initiation of PD and patients who started PD for other reasons, such as congestive heart failure or acute renal failure, were excluded from the study.

The HD treatment was performed three‐times weekly with a dialysis time of 3.5–4 h per session, a filter of 1.5–2 m2 surface area by high‐flux synthetic membrane, defined by a ultrafiltration coefficient >20 ml/h, [17] and a blood flow of 350–400 ml/min. A bicarbonate‐based ultrapure buffer dialysis solution was used with a dialysate flow rate of 500–600 ml/min, a calcium concentration of 1.50–1.75 mmol/L, a sodium concentration of 138–145 mmol/L, and low molecular weight heparin as anticoagulant therapy. The final concentration of bicarbonate in dialysate was 32 mEq/L. Dialysis dose was defined by Kt/V/day for urea which was calculated according to the formula of Daugirdas. [18] Patients were excluded if they had Kt/V for urea <1.2.

The included PD patients were following continuous ambulatory PD with 4 changes/day using a combination of 2 changes of 2 L of hypertonic glucose‐based solution (3.86% glucose; Baxter Healthcare) and 2 changes of 2 L of semihypertonic glucose solution (2.5% glucose; Ariti; Bieffe Medital S.P.A). All patients underwent urea kitenic analysis including residual renal function every 3 months of PD initiation. Dialysis dose defined according to the formula of Daugirdas by total Kt/V/week for urea including peritoneal Kt/V urea and residual GFR (ml/min/1.73 m2). The patients who had Kt/V/week for urea <1.7 were excluded from our study. We used peritoneal liquids in dual backs with a final concentration of bicarbonate equal to 37.5 mEq/L. The enrolled patients were in a good status, they did not have interdialytic peripheral edema, high blood pressure, interdialytic orthostatic hypotension, or other characteristics of an inaccurate dry body weight. However, patients with predialysis blood pressure ≥140/90 (n = 40, a ratio of 41.7%) were considered hypertensive or if they were receiving antihypertensive drugs.

Blood collection

Blood samples were obtained by venipuncture in the PD patients in a 12 h fasting state during an regular appointment in our peritoneal unit. In HD patients, blood was drawn just before the start of the mean weekly dialysis session also in a 12 h fasting state from the vascular access. In the end of the treatment, the blood pump speed was reduced to <80 ml/min and blood samples was obtained at 2 min post dialysis from the arterial dialysis tubing for the calculation of the adequacy of dialysis by Kt/V for urea. Samples were centrifuged immediately; serum was separated and processed for various assays. In each subject, three sequences of samples (every month within 3 months) were received for the serum bicarbonate measurements, and their average was used for statistical analysis.

Laboratory measurements

Albumin, high‐density lipoproteins (HDLs), and low‐density lipoproteins (LDLs) were measured by biochemical analysis and the ratio of LDL/HDL was calculated. High‐sensitivity C‐reactive protein (hsCRP) and oxidized LDL (ox‐LDL) serum concentrations were measured using enzyme‐linked immunosorbent assays (Immundiagnostik AG, Germany and Immundiagnostik AG. Stubenwald‐Allee, Bensheim, respectively) according to manufacturer's specifications. The concentrations of intact parathormone (i‐PTH) and beta‐2‐microglobulin (beta2M) were measured by radioimmunoassays. Insulin levels were measured using a immunoradiometric assay with a reported interassay coefficient of variation 6.1%. Insulin resistance (IR) was calculated using the homeostasis model assessment of insulin resistance (HOMA‐IR). [19]

Metabolic acidosis was defined by serum bicarbonate concentrations <22 mEq/L, which were measured in gas machine

(Roche, cobas b 121) taking care of the blood specimens. [20] The low serum bicarbonate level was considered in combination to low arterial pH (acidemia) and decreased PCO2, thus the decreased serum bicarbonate concentrations to reflect metabolic acidosis rather than respiratory alkalosis. Respiratory alkalosis is another clinical condition that causes decreased bicarbonate level in the end‐stage of renal disease (ESRD) patients, due to the loss of buffering capacity by the kidney in these patients. Normalized protein catabolic rate for dry body mass was calculated from the urea generation rate. [21] Body mass index (BMI) was obtained from height and post dialysis body weight.

Hemodynamic measurements

Predialysis peripheral systolic blood pressure and diastolic blood pressures (SBP and DBP, respectively) in enrolled patients were calculated as the mean of 10 measurements during a treatment month using an automatic sphygmomanometer OMRON M4‐I (Co., Ltd. Kyoto, Japan). Mean peripheral predialysis BP (MBP) was calculated as MBP = DBP + 1/3 (SBP − DBP). Electrocardiographical analysis and M‐mode echocardiography were performed the day after dialysis with an Hewlett Packard, SONOS 2500 using a 2.25 MHz transducer to estimate the ejection fraction and the ischemic findings according to the recommendations of the American Society of Echocardiography. [22]

Arterial stiffness was measured as carotid‐femoral pulse wave velocity (c‐f PWV) and carotid augmentation index (AIx) using the SphygmoCor System® (AtCor Medical Pty. Ltd, Sydney, Australia). In each subject, two sequences of measurements were performed, and their mean was used for statistical analysis. We recorded the c‐f PWV by positioning one sensor over the right femoral artery and a second sensor over the left carotid artery. The distance between the two sensors was measured with a measuring tape, and three recordings of both pulse waveforms were performed (8–10 heart beats for each recording). The Complior software (Colson, Garges les Genosse, France, Software version 2.1) automatically detected the foot of each pulse waveform from the two arterial sites and then measured the mean distance between the two feet as being the travel time of the wave. PWV was then computed using the formula: PWV = travel distance/ travel time as previously validated. [23] Central SBP, DBP, MBP, pulse pressure (PP), and the time of return of the reflected wave (Tr) were derived. Pressure and time of first peak (P1 and T1) and second peak (P2 and T2) and central augmented pressure (AP) were obtained. Central AIx was computed (AP = P2 − P1; AIx = [AP/PP] × 100) and corrected for a heart rate of 75 beats/min.

Data analysis

Data were analyzed using SPSS version 15.0 statistical package for Windows (SPSS Inc., Chicago, Illinois, USA) and expressed as mean ± standard deviation or as median value (interquartile range) for data that showed skewed distribution; differences between mean values were assessed using unpaired t‐test for two groups and data that showed skewed distributions were compared with Mann–Whitney U‐test.

Results

Table 1: Demographical characteristics of studied patients

Variable	N%
Gender	
Male	66 (66)
Female	34 (34)

Diabetes mellitus	10 (10)
Hypertension	40 (40)
Current smoking	30 (30)
Coronary artery disease	30 (30)
Hemodiafiltration/peritoneal dialysis	80 (80)
Serum bicarbonate	
> 22 mEq/L	32 (32)
<22 mEq/L	68 (68)
Mortality rate during total dialysis vintage	
Alive	70 (70)
Dead	30 (30)

We studied 100 dialysis patients, 66 males and 34 females, on mean age 62.1 ± 14.27 years old. The treatment modalities which were applied were predilution hemodiafiltration (HDF, n = 80), and peritoneal dialysis (PD, n = 20). 80% were with Hemodiafiltration/peritoneal dialysis, 40 5 were having hypertension, 30% were having CAD.

Table 2: Differences between groups of patients according to the existence of coronary artery disease

Characteristic	Patients with CAD (n=30)	Patients without CAD (n=70)
Age (years)	68.9±10.3	59.0±14.7
BMI (kg/m2)	24.9±2.6	25.1±4.3
LDL/HDL	2.1±0.8	2.5±0.9
HOMA-IR (mmol/L)	5.5±4.5	6.0±7.4
Beta2M (mg/L)	40.2±34.9	29.5±23.6
Serum bicarbonate (mEq/L)	19.7±2.7	20.9±2.5
i-PTH (pg/ml)	245.9±203.9	196.7±229.2
hsCRP (mg/L)	10.3±6.1	7.9±5.7
ox-LDL (ng/ml)	165.0±240.9	89.1±87.0
Albumin (g/dl)	3.7±0.6	3.93±0.3
MBP (mmHg)	99.0±14.4	97.2±13.7
c-f PWV (m/s)	12.2±1.7	10.8±1.7
AIx	25.06±1.9	23.7±2.4
PP (mmHg)	64.1±21.8	54.01±19.3

The differences between the groups of patients with CAD manifestation or without CAD are shown. We observed that the patients with CAD had higher age, beta2M, i‑PTH, c‑f PWV, PP, AIx, ox‑LDL, and hsCRP but lower serum bicarbonate concentrations, BMI, and albumin than the patients without manifested CAD.

Table 3: Differences between groups of patients according to dialysis modality

Characteristic	Patients on hemodiafiltration N=80	Patients on peritoneal dialysis N=20
Age (years)	62.2±15.0	61.6±11.3
BMI (kg/m2)	24.4±3.0	27.4±5.5
Urine volume (ml/day)	229.3±153.8	517.8±384.6
Serum bicarbonate	20.09±2.2	22.08±2.8

(mEq/L)		
i-PTH (pg/ml)	180.4±189.2	332.2±292.1
HOMA-IR (mmol/L)	5.3±5.1	7.7±10.7
Beta2M (mg/L)	33.9±31.1	28.7±7.6
Albumin (g/dl)	3.9±0.4	3.5±0.4
hsCRP (mg/L)	7.9±5.8	11.2±5.8
oxLDL (ng/ml)	129.7±170.6	48.4±18.1
MBP (mmHg)	98.4±12.6	95.2±18.08
c-f PWV (m/s)	11.3±1.8	11.2±2.0
AIx	24.1±2.1	24.1±2.9
PP (mmHg)	58.2±19.2	53.2±24.9

We noted that the patients on HDF had lower i‑PTH, serum bicarbonate levels, hsCRP, IR defined by HOMA‑IR but higher albumin, ox‑LDL, and beta2M than the patients on PD.

Table 4: Differences between groups of patients according to lower or higher than 22 mEq/L serum bicarbonate level

Characteristic	Patients with serum bicarbonate <22mEq/L (n=68)	Patients with serum bicarbonate >22 mEq/L (n=32)
Age (years)	61.5±13.8	53.9±14.5
BMI (kg/m2)	25.2±4.3	25.3±3.8
Urine volume (ml/day)	308.8±223.7	436.15±406.0
Serum bicarbonate (mEq/L)	19.2±1.9	23.3±1.2
HOMA‑IR (mmol/L)	6.9±8.7	4.9±3.5
Beta2M (mg/L)	29.9±22.3	26.1±9.5
i‑PTH (pg/ml)	262.9±280.1	166.1±132.7
Albumin (g/dl)	3.8±0.3	3.9±0.4
LDL/HDL	2.4±1.04	2.5±0.7
hsCRP (mg/L)	9.5±5.8	6.6±5.9
Ox‑LDL (ng/ml)	127.5±175.6	84.1±85.8
MBP (mmHg)	96.3±12.6	94.6±15.9
c‑f PWV (m/s)	11.5±1.8	10.3±1.9
AIx	24.6±2.3	23.0±2.7
PP (mmHg)	55.9±21.1	49.9±18.9

We observed that the patients with serum bicarbonate levels <22 mEq/L were older, they had higher beta2M, HOMA‑IR, i‑PTH, hsCRP, ox‑LDL, c‑f PWV, PP, and AIx, but lower albumin level and lower urine volume in comparison to the patients with serum bicarbonate levels >22 mEq/L.

Discussion

Ideal management strategies before and at the initiation of dialysis to optimize the transition to ESRD and improve outcomes have not been well defined. [23] Although overall mortality rates of the ESRD population are improving, the immediate period after transition to ESRD is associated with the highest mortality rates. Mortality rates up to 30% have been described within the first year of transition from CKD to ESRD. [24,25]

Increased PWV and AIx are integrated indexes of vascular function and structure. They estimate the arterial stiffness, which is a strong predictor of cardiovascular

mortality in general population and in dialysis patients. [26] Furthermore, elevated PP is one another consequence of arterial stiffening and vascular calcification. Previously, it has been shown the positive relationship between the extent of vascular calcification and arterial stiffness and it may explain the increased cardiovascular events seen in dialysis patients. [27] In addition, it has been already established that ESRD results in accelerated atherosclerosis and increased morbidity and mortality. [15] Even when the patients are undergoing renal replacement therapy, the mortality remains high, mainly for cardiovascular causes due either to uremia‐related risk factors (such as anemia, hyperparathyroidism, inflammation, oxidative stress, and malnutrition) [28,29] or to traditional ones (age, male gender, diabetes, obesity, hypertension, smoking, dyslipidemia). [30,31] Indeed, in the present study, the patients with manifested CAD were older and they had higher i‐PTH, hsCRP, ox‐LDL, beta2M, and worse status of metabolic acidosis in combination to lower albumin and BMI, which are some of the malnutrition characteristics, than the patients without CAD.

In addition, in this study, we observed that the patients with low bicarbonate level (<22 mEq/L) had higher c‐f PWV, AIx, PP, beta2M, IR defined by increased HOMA‐IR, i‐PTH, hsCRP, ox‐LDL, but lower albumin level and lower urine volume as an indicator of decreased residual renal function, than the patients with serum bicarbonate levels >22 mEq/L. These findings support that metabolic acidosis results in detrimental effects and patients with low bicarbonate level should be treated properly even though they are receiving dialysis therapy. Previously, it has already been reported the role of metabolic acidosis on vascular calcification as the mineral metabolism disturbances act through the existing metabolic acidosis in dialysis patients. The influence of acidosis on vascular calcification is complicated, acting as a stimulator of the solubility of Ca x P deposits and as a blocker of phosphate uptake by the arterial smooth muscle cells, so acidosis may attenuate vascular calcification. [32]

Previous study showed that serum bicarbonate level >22 mEq/L was associated with lower mortality risk[30] and another study reported that an increased risk was observed in patients with high (>27 mEq/L) or low (<17 mEq/L) bicarbonate levels.33 In this study, we were considered uncorrected metabolic acidosis in enrolled patients, when serum bicarbonate level was <22 mEq/L combined to low arterial pH and decreased PCO2. Therefore, the low bicarbonate level may be diagnostic of metabolic acidosis rather than of respiratory alkalosis, another clinical condition that causes decreased bicarbonate level, given the loss of buffering capacity by the kidney in ESRD. However, in our data, the mean value of serum bicarbonate concentrations, particularly for enrolled patients on HDF, was lower comparatively to previous reports, [33] due may to the differently used bicarbonate concentration in dialysis dialysate. Furthermore, we did not exclude from the study the diabetic patients who may have worse metabolic acidosis state in our baseline measurements. Moreover, in this study, the dialysis modality showed a significant influence on mortality rate notifying that the patients on PD presented worse survival than the patients on HDF despite dialysis modality was not significantly associated with the existence of CAD, neither with low bicarbonate level by Kaplan–Meier curves during our follow‐up time of 60 months. Specifically, during the first 28–30 months from treatment initiation, the survival was better for PD; but then, the mortality was significantly increased comparatively to the patients on HDF. [34]

Conclusion

Uncorrected metabolic acidosis and CAD were shown as independent significant predictors for mortality in patients on renal replacement therapy. PD may provide worse survival after 2–2.5 years of treatment initiation than HDF.

References

1. Franch HA, Mitch WE. Catabolism in uremia: the impact of metabolic acidosis. Journal of the American Society of Nephrology: JASN. 1998 Dec 1;9(12 Suppl): S78-81.
2. Kalantar-Zadeh K, Mehrotra R, Fouque D, Kopple JD. Poor Nutritional Status and Inflammation: Metabolic Acidosis and Malnutrition-Inflammation Complex Syndrome in Chronic Renal Failure. In Seminars in dialysis. Oxford, UK: Blackwell Science Inc. 2004 Nov; 17(6): 455-465.
3. Uribarri J, Levin NW, Delmez J, Depner TA, Ornt D, Owen W, Yan G, Hemodialysis Study Group. Association of acidosis and nutritional parameters in hemodialysis patients. American journal of kidney diseases. 1999 Sep 1;34(3):493-9.
4. Kopple JD, Kalantar-Zadeh K, Mehrotra R. Risks of chronic metabolic acidosis in patients with chronic kidney disease. Kidney International. 2005 Jun 1;67: S21-7.
5. Korbet SM, Schwartz MM, Lewis EJ. American journal of kidney diseases: the official journal of the National Kidney Foundation. Am J Kidney Dis. 1994;23(6):773-83.
6. Vashistha T, Kalantar-Zadeh K, Molnar MZ, Torlen K, Mehrotra R. Dialysis modality and correction of uremic metabolic acidosis: relationship with all-cause and cause-specific mortality. Clinical journal of the American Society of Nephrology. 2013 Feb 1;8(2):254-64.
7. Bommer J, Locatelli F, Satayathum S, Keen ML, Goodkin DA, Saito A, Akiba T, Port FK, Young EW. Association of predialysis serum bicarbonate levels with risk of mortality and hospitalization in the Dialysis Outcomes and Practice Patterns Study (DOPPS). American journal of kidney diseases. 2004 Oct 1;44(4):661-71.
8. Wu DY, Kilpatrick RD, Dadres S, McAllister CJ, Kopple JD, Kalantar-Zadeh K. Association between serum bicarbonate and death in hemodialysis patients: is it better to be acidotic or alkalotic? Hemodialysis International. 2005 Jan;9(1):87-.
9. Lowrie EG, Lew NL. Death risk in hemodialysis patients: the predictive value of commonly measured variables and an evaluation of death rate differences between facilities. American Journal of Kidney Diseases. 1990 May 1;15(5):458-82.
10. Grassmann A, Gioberge S, Moeller S, Brown G. ESRD patients in 2004: global overview of patient numbers, treatment modalities and associated trends. Nephrology dialysis transplantation. 2005 Dec 1;20(12): 25 87-93.
11. de Jager DJ, Grootendorst DC, Jager KJ, van Dijk PC, Tomas LM, Ansell D, Collart F, Finne P, Heaf JG, De Meester J, Wetzels JF. Cardiovascular and noncardiovascular mortality among patients starting dialysis. Jama. 2009 Oct 28;302(16):1782-9.
12. McIntyre CW. Effects of hemodialysis on cardiac function. Kidney international. 2009 Aug 2;76(4):371-5.
13. Vonesh EF, Snyder JJ, Foley RN, Collins AJ. Mortality studies comparing peritoneal dialysis and hemodialysis: what do they tell us? Kidney International. 2006 Nov 1;70: S3-11.
14. Wu B, Wang M, Gan L, Zhao H. Comparison of patient survival between hemodialysis and peritoneal dialysis in a single Chinese center.

International urology and nephrology. 2014 Dec; 46:2403-7.
15. Guérin AP, Pannier B, Marchais SJ, London GM. Cardiovascular disease in the dialysis population: prognostic significance of arterial disorders. Current opinion in nephrology and hypertension. 2006 Mar 1;15(2):105-10.
16. Chang TI, Kang EW, Kim HW, Ryu GW, Park CH, Park JT, Yoo TH, Shin SK, Kang SW, Choi KH, Han DS. Low serum bicarbonate predicts residual renal function loss in peritoneal dialysis patients. Medicine. 2015 Aug;94(31).
17. Chauveau P, Nguyen H, Combe C, Chêne G, Azar R, Cano N, Canaud B, Fouque D, Laville M, Leverve X, Roth H. Dialyzer membrane permeability and survival in hemodialysis patients. American journal of kidney diseases. 2005 Mar 1;45(3):565-71.
18. Daugirdas JT. Second generation logarithmic estimates of single-pool variable volume Kt/V: an analysis of error. Journal of the American Society of Nephrology. 1993 Nov 1;4(5):1205-13.
19. Silva EA, Flexa F, Zanella MT. Impact of abdominal fat and insulin resistance on arterial hypertension in non-obese women. Arquivos Brasileiros de Endocrinologia & Metabologia. 2009; 53:340-3.
20. Kirschbaum B. Spurious metabolic acidosis in hemodialysis patients. American Journal of Kidney Diseases. 2000 Jun 1;35(6):1068-71.
21. Daugirdas JT. Simplified equations for monitoring Kt/V, PCRn, eKt/V, and ePCRn. Advances in renal replacement therapy. 1995 May 1;2(4):295-304.
22. Nitta K, Kawashima A, Yumura W, Naruse M, Oba T, Kabaya T, Nihei H. Plasma concentration of brain natriuretic peptide as an indicator of cardiac ventricular function in patients on hemodialysis. American journal of nephrology. 1998;18(5):411-5.
23. Kalantar-Zadeh K, Kovesdy CP, Streja E, Rhee CM, Soohoo M, Chen JL, Molnar MZ, Obi Y, Gillen D, Nguyen DV, Norris KC. Transition of care from pre-dialysis prelude to renal replacement therapy: the blueprints of emerging research in advanced chronic kidney disease. Nephrology Dialysis Transplantation. 2017 Apr 1;32 (sup l_2): ii91-8.
24. Saran R, Robinson B, Abbott KC, et al. US Renal Data System 2016 Annual Data Report: Epidemiology of Kidney Disease in the United States. Am J Kidney Dis. 2017;69: A7–A8.
25. Foley RN, Chen SC, Solid CA, Gilbertson DT, Collins AJ. Early mortality in patients starting dialysis appears to go unregistered. Kidney international. 2014 Aug 1;86(2):392-8.
26. London GM, Blacher J, Pannier B, Guérin AP, Marchais SJ, Safar ME. Arterial wave reflections and survival in end-stage renal failure. Hypertension. 2001 Sep 1;38(3):434-8.
27. Raggi P, Bellasi A, Ferramosca E, Islam T, Muntner P, Block GA. Association of pulse wave velocity with vascular and valvular calcification in hemodialysis patients. Kidney international. 2007 Apr 2;71(8):802-7.
28. Gleissner CA, Leitinger N, Ley K. Effects of native and modified low-density lipoproteins on monocyte recruitment in atherosclerosis. Hypertension. 2007 Aug 1;50(2):276-83.
29. Hansson GK, Robertson AK, Söderberg-Nauclér C. Inflammation and atherosclerosis. Annu. Rev. Pathol. Mech. Dis. 2006 Feb 28; 1:297-329.
30. Wen CP, Cheng TY, Tsai MK, Chang YC, Chan HT, Tsai SP, Chiang PH, Hsu CC, Sung PK, Hsu YH, Wen SF. All-cause mortality attributable to chronic kidney disease: a prospective cohort study based on 462 293 adults in Taiwan. The lancet. 2008 Jun 28; 371(9631):2173-82.

31. Stenvinkel P, Heimbürger O, Paultre F, Diczfalusy U, Wang T, Berglund L, Jogestrand T. Strong association between malnutrition, inflammation, and atherosclerosis in chronic renal failure. Kidney international. 1999 May 1;55(5):1899-911.
32. Yonova D. Vascular calcification and metabolic acidosis in end stage renal disease. Hippokratia. 2009 Jul; 13(3):139.
33. Bommer J, Locatelli F, Satayathum S, Keen ML, Goodkin DA, Saito A, Akiba T, Port FK, Young EW. Association of predialysis serum bicarbonate levels with risk of mortality and hospitalization in the Dialysis Outcomes and Practice Patterns Study (DOPPS). American journal of kidney diseases. 2004 Oct 1;44(4):661-71.
34. Manfred D. May There Exist Healthy Diseases? Journal of Medical Research and Health Sciences. 2022; 5(3): 1801–1803.