Original Article

# Seasonal Variations of Clinical and Biochemical Parameters in Chronic Haemodialysis

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## Abstract

**Introduction: Seasonal variations in clinical and laboratory variables occur commonly among chronic haemodialysis patients. In order to demonstrate seasonal differences, we prospectively compared biochemical and clinical parameters in a group of chronically haemodialysed patients living in South Croatia, a region with a Mediterranean climate. Materials and Methods: Data were processed on 135 single dialysis treatments involving a group of 34 anuric chronic haemodialysis (HD) patients. Outcomes were measured at 3-month intervals, in March, June, September and December. Results: The seasonal differences were found in phosphorus (*P* = 0.001), creatinine before HD (*P* <0.001), creatinine after HD (*P* = 0.005), alkaline phosphatase (*P* = 0.012), alanine aminotransferase (*P* = 0.042), urea before HD (*P* = 0.039), albumins (*P* <0.001), total cholesterol (*P* <0.001), low-density lipoprotein (LDL) cholesterol (*P* <0.001), high-density lipoprotein (HDL) cholesterol (*P* <0.001), glucose (*P* = 0.033), and ultrafiltration per HD (*P* = 0.037). When the data were grouped into cold (March and December) and mild (June and September) months, we found differences in phosphorus (1.48 ± 0.47 versus 1.72 ± 0.51, *P* = 0.005), alkaline phosphatase (119.46 ± 69.03 versus 169.78 ± 107.98, *P* = 0.002), urea before HD (27.13 ± 5.35 versus 24.40 ± 5.99, *P* = 0.006), albumins (37.92 ± 5.17 versus 40.58 ± 5.69, *P* = 0.006), total cholesterol (4.93 ± 0.93 versus 5.30 ± 0.93, *P* = 0.023), LDL cholesterol (2.85 ± 1.04 versus 3.23 ± 0.87, *P* = 0.046), glucose (4.62 ± 1.15 versus 5.57 ± 1.46, *P* = 0.004), and ultrafiltration per HD (3.57 ± 1.18 versus 2.97 ± 1.20, *P* = 0.004). Conclusion: In Mediterranean climates, seasonal differences in predialysis urea concentration and ultrafiltration rate per dialysis could be attributed to different food and water intake. The seasonal differences in blood concentration of phosphorus, alkaline phosphatase, total cholesterol, LDL cholesterol, and glucose might be the results of neurohormonal influences. This climate has no impact on haemoglobin and blood pressure levels.**


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**Key words: Chronic kidney failure, Metabolism, Nutrition, Seasonal variation**

## Introduction

Seasonal variations in the general population in some body functions and diseases incidences have been well-established (e.g., vitamin D levels, allergic rhinitis, blood pressure, levels of physical activity and energy expenditure, mental depression, peptic ulcer disease, and death from chronic heart failure).[1-5] Similar patterns of seasonal variations in some clinical and laboratory variables occur commonly among chronic haemodialysis patients and these variables correlate mostly with ambient temperature and relative humidity.[6] The reasons for most of these variations are not apparent and require further investigation. For example, blood pressure has a seasonal cycle in the general population and in patients undergoing maintenance dialysis, but the causes remain unclear. This has important therapeutic, research, and epidemiological implications. As some of the seasonal variations of biochemical and clinical parameters among patients on chronic haemodialysis correlate with ambient temperature and humidity, these variations could be different in various climates. The

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chronically haemodialysed patients in Europe have not been comprehensively investigated with regard to seasonal variations in clinical and biochemical parameters.

In order to demonstrate seasonal differences, we prospectively compared biochemical and clinical parameters in a group of chronically haemodialysed patients living in South Croatia, a region with a Mediterranean climate. This climate is characterised by mild winters and hot summers with high relative humidity.

## Materials and Methods

Data were processed on 135 single dialysis treatments involving a group of 34 anuric chronic haemodialysis patients (18 males and 16 females) who were on a thrice-weekly dialysis regimen and had been receiving chronic haemodialysis treatment for at least 1 year in a South Croatian coastal outhospital haemodialysis centre.

The overall study period was 9 months. Outcomes were measured at study initiation and then at 3-month intervals; 4 measurements per subject were obtained (in March, June, September, and in December).

Primary outcome measures for every single observed haemodialysis (HD) included the blood concentrations of urea before and after haemodialysis (mmol/L), haemoglobin (g/L), calcium, phosphorus (mmol/L), total protein and albumin in serum (g/L), glucose (mmol/L), aspartate aminotransferase, alanin aminotransferase, γ-glutamyl transpeptidase, alkaline phosphatase (IU/L), creatinine before and after HD (mmol/L), total cholesterol, low-density lipoprotein (LDL)-cholesterol, high-density lipoprotein (HDL)-cholesterol, triglycerides (mmol/L). In addition, the number of blood leukocytes and erythrocytes, systolic and diastolic blood pressure before and after HD (mmHg), and ultrafiltration (L) and body mass before and after HD (kg) were observed.

Secondary outcome measures were single dialysis efficacy (Kt/V) calculated according to Daugirdas second-generation formula[7] and predialysis and postdialysis mean arterial pressure (MAP) calculated as (systolic +2 diastolic blood pressure)/3 (mm Hg).

The parameters of the haemodialysis treatments were as follows: 3.5 hours to 5 hours, mean heparinisation dose 45,258 ± 1078 IU, temperature of the dialysis bath 35.5°C to 36.6°C. The dialysate bath consisted of bicarbonate 33 to 35 mmol/L, sodium 138 to 143 mmol/L, potassium 2 mmol/L, and calcium 1.25 to 1.75 mmol/L. The subjects were dialysed on low flux polysulphone dialysers (F6 and F8, Fresenius, Bad Homburg, Germany). All subjects had Cimino fistula as their blood access. All subjects were treated with erythropoietin in average weekly subcutaneous doses of 3622 ± 1856 IU.

Blood was taken just prior to connecting the subject to the dialysis machine and before administering heparin. For determining the postdialysis blood urea concentration, a blood sample was obtained from the arterial line 2 minutes after the blood pump was reduced to 50 mL/min (slow-flow technique).

During each dialysis, conditions for the same subject were unchanged. If the prescribed conditions during dialysis treatment were changed, that dialysis session was not included in the study. Conditions did change during 1 dialysis treatment; thus, 135 dialyses were included in the investigation.

Haematological and biochemical parameters were measured using routine laboratory methods. Triglycerides, total cholesterol, and HDL cholesterol were analysed with enzymatic kits, and LDL cholesterol was calculated according to Friedewald's equation.[8] Ultrafiltration was measured volumetrically on the dialysis machines.

The results are expressed as the arithmetic mean ± standard deviation. Differences between 4 groups were tested with one-way analysis of variances (ANOVA) with Bonferroni post hoc tests. Differences between 2 groups were calculated by Student's *t*-test for independent data. A *P* value of less than 0.05 was considered to be statistically significant.

## Results

The overall study data from the 135 dialysis treatments are shown in Table 1. Significant seasonal differences were found in phosphorus ($P = 0.001$), creatinine before HD ($P < 0.001$), creatinine after HD ($P = 0.005$), alkaline phosphatase ($P = 0.012$), alanine aminotransferase ($P = 0.042$), urea before HD ($P = 0.039$), albumin ($P < 0.001$), total cholesterol ($P < 0.001$), LDL cholesterol ($P < 0.001$), HDL cholesterol ($P < 0.001$), glucose ($P = 0.033$), and ultrafiltration per HD ($P = 0.037$). For these variables, Bonferroni post hoc tests were performed and the results are shown in Table 2.

When the data were grouped into 2 groups of cold (March and December) and mild (June and September) months, we tested differences between the groups with Student's *t*-test for independent data (Table 3). There were significant differences between cold and mild months in the levels of phosphorus (1.48 ± 0.47 versus1.72 ± 0.51, $P = 0.005$), alkaline phosphatase (119.46 ± 69.03 versus 169.78 ± 107.98, $P = 0.002$), urea before HD (27.13 ± 5.35 versus 24.40 ± 5.99, $P = 0.006$), albumins (37.92 ± 5.17 versus 40.58 ± 5.69, $P = 0.006$), total cholesterol (4.93 ± 0.93 versus 5.30 ± 0.93, $P = 0.023$), LDL cholesterol (2.85 ± 1.04 versus 3.23 ± 0.87, $P = 0.046$), glucose (4.62 ± 1.15 versus 5.57 ± 1.46, $P = 0.004$), and ultrafiltration per HD (3.57 ± 1.18 versus 2.97 ± 1.20, $P = 0.004$).

Table 1. Seasonal Variations in Biochemical and Clinical Parameters in 135 Haemodialysis Sessions Performed on 34 Chronic Haemodialysis Patients (ANOVA)

| | March | June | September | December | Total | *P* |
|---|---|---|---|---|---|---|
| Number of HD | 34 | 34 | 34 | 33 | 135 | |
| Calcium (mmol/L) | 2.56 ± 0.26 | 2.57 ± 0.25 | 2.58 ± 0.19 | 2.64 ± 0.23 | 2.58 ± 0.24 | 0.598 |
| Phosphorus (mmol/L) | 1.59 ± 0.52 | 1.79 ± 0.50 | 1.58 ± 0.50 | 1.27 ± 0.25 | 1.60 ± 0.50 | 0.001* |
| Creatinine before HD (mmol/L) | 1.27 ± 0.30 | 1.38 ± 0.34 | 1.04 ± 0.22 | 1.22 ± 0.28 | 1.26 ± 0.32 | <0.001* |
| Creatinine after HD (mmol/L) | 0.47 ± 0.13 | 0.55 ± 0.16 | 0.44 ± 0.11 | 0.55 ± 0.16 | 0.50 ± 0.15 | 0.005* |
| Erythrocytes number (*$10^{12}$) | 3.44 ± 0.48 | 3.42 ± 0.45 | 3.56 ± 0.48 | 3.34 ± 0.48 | 3.44 ± 0.47 | 0.451 |
| Haemoglobin (g/L) | 107.82 ± 13.19 | 109.8 ± 13.15 | 116.39 ± 13.75 | 109.87 ± 14.07 | 110.32 ± 13.59 | 0.103 |
| Alkaline phosphatase (IU/L) | 113.18 ± 60.15 | 164.33 ± 91.70 | 180.43 ± 136.07 | 131.48 ± 83.63 | 144.81 ± 93.89 | 0.012* |
| Aspartate aminotransferase (IU/L) | 9.80 ± 5.03 | 11.47 ± 11.11 | 10.35 ± 7.77 | 11.09 ± 5.63 | 10.66 ± 8.03 | 0.790 |
| Alanine aminotransferase (IU/L) | 15.02 ± 5.29 | 17.20 ± 15.02 | 21.83 ± 7.71 | 19.95 ± 4.05 | 17.73 ± 10.12 | 0.042* |
| γ-glutamyl transpeptidase (IU/L) | 21.32 ± 9.64 | 24.00 ± 27.70 | 20.30 ± 10.84 | 22.50 ± 16.50 | 22.24 ± 18.67 | 0.862 |
| Urea before HD (mmol/L) | 27.48 ± 5.83 | 24.73 ± 5.93 | 23.78 ± 6.18 | 26.47 ± 4.34 | 25.77 ± 5.82 | 0.039* |
| Urea after HD (mmol/L) | 9.96 ± 2.78 | 9.53 ± 3.32 | 8.46 ± 2.48 | 10.62 ± 3.22 | 9.67 ± 3.04 | 0.092 |
| Total proteins (g/L) | 66.17 ± 4.59 | 66.72 ± 4.66 | 68.67 ± 4.96 | 66.20 ± 5.82 | 66.79 ± 4.93 | 0.228 |
| Albumins (g/L) | 37.63 ± 5.41 | 42.42 ± 4.67 | 37.13 ± 5.90 | 38.48 ± 4.74 | 39.25 ± 5.57 | <0.001* |
| Total cholesterol (mmol/L) | 5.22 ± 0.88 | 5.22 ± 0.96 | 5.44 ± 0.87 | 4.38 ± 0.77 | 5.11 ± 0.94 | <0.001* |
| LDL (mmol/L) | 3.30 ± 0.93 | 3.07 ± 0.98 | 3.40 ± 0.73 | 1.99 ± 0.60 | 3.00 ± 0.99 | <0.001* |
| HDL (mmol/L) | 1.10 ± 0.34 | 1.28 ± 0.50 | 1.19 ± 0.22 | 1.71 ± 0.42 | 1.28 ± 0.44 | <0.001* |
| Triglycerides (mmol/L) | 2.29 ± 1.06 | 2.30 ± 0.97 | 2.08 ± 0.68 | 2.08 ± 0.83 | 2.22 ± 0.93 | 0.654 |
| Glucose (mmol/L) | 4.64 ± 0.98 | 5.59 ± 1.51 | 5.46 ± 1.36 | 4.60 ± 1.33 | 5.03 ± 1.37 | 0.033* |
| Leukocytes number (*$10^{9}$) | 6.31 ± 1.96 | 6.40 ± 1.97 | 6.58 ± 1.74 | 6.69 ± 1.87 | 6.45 ± 1.90 | 0.866 |
| Systolic BP before HD (mmHg) | 144.61 ± 27.99 | 144.84 ± 27.83 | 142.13 ± 24.84 | 148.43 ± 26.33 | 144.92 ± 26.91 | 0.888 |
| Diastolic BP before HD (mmHg) | 78.50 ± 14.95 | 78.42 ± 13.23 | 81.30 ± 15.67 | 81.17 ± 16.74 | 79.41 ± 14.74 | 0.786 |
| Systolic BP after HD (mmHg) | 133.91 ± 26.63 | 134.93 ± 30.71 | 134.78 ± 25.55 | 132.13 ± 25.94 | 134.10 ± 27.49 | 0.982 |
| Diastolic BP after HD (mmHg) | 75.36 ± 15.34 | 73.67 ± 14.61 | 71.48 ± 11.54 | 71.91 ± 14.80 | 73.55 ± 14.34 | 0.690 |
| Body mass before HD (kg) | 75.75 ± 12.76 | 74.10 ± 13.40 | 74.67 ± 13.26 | 74.76 ± 13.72 | 74.85 ± 13.09 | 0.950 |
| Body mass after HD (kg) | 72.59 ± 12.35 | 71.49 ± 12.63 | 72.24 ± 12.59 | 71.57 ± 13.40 | 71.99 ± 12.53 | 0.977 |
| Ultrafiltration per HD (L) | 3.58 ± 1.19 | 3.03 ± 1.30 | 2.86 ± 1.00 | 3.55 ± 1.20 | 3.27 ± 1.22 | 0.037* |
| Kt/V | 1.27 ± 0.24 | 1.20 ± 0.33 | 1.25 ± 0.22 | 1.17 ± 0.28 | 1.22 ± 0.28 | 0.461 |
| MAP before HD (mmHg) | 100.54 ± 18.00 | 100.56 ± 17.04 | 101.58 ± 17.73 | 103.59 ± 18.12 | 101.24 ± 17.50 | 0.907 |
| MAP after HD (mmHg) | 94.88 ± 17.36 | 94.09 ± 19.28 | 92.58 ± 15.01 | 91.99 ± 17.25 | 93.73 ± 17.49 | 0.913 |

*$P$ <0.05

BP: blood pressure; HD: haemodialysis; HDL: high-density lipoproteins; LDL: low-density lipoproteins; Kt/V: single dialysis efficiency; MAP: mean arterial pressure

Table 2. The Sets of Bonferroni Post Hoc Tests Performed for Variables with Significant Seasonal Differences

| | March | June | September | December | *P* (ANOVA) |
|---|---|---|---|---|---|
| Number of HD | 34 | 34 | 34 | 33 | |
| Phosphorus (mmol/L) | 1.59 ± 0.52[a] | 1.79 ± 0.50[b] | 1.58 ± 0.50 | 1.27 ± 0.25[a,b] | 0.001* |
| Creatinine before HD (mmol/L) | 1.27 ± 0.30[c] | 1.38 ± 0.34[b] | 1.04 ± 0.22[c,b] | 1.22 ± 0.28 | <0.001* |
| Creatinine after HD (mmol/L) | 0.47 ± 0.13[a] | 0.55 ± 0.16[a,d] | 0.44 ± 0.11[d,e] | 0.55 ± 0.16[e] | 0.005* |
| Alkaline phosphatase (IU/L) | 113.18 ± 60.15[f,g] | 164.33 ± 91.70[f] | 180.43 ± 136.07[g] | 131.48 ± 83.63 | 0.012* |
| Alanine aminotransferase (IU/L) | 15.02 ± 5.29[h] | 17.20 ± 15.02 | 21.83 ± 7.71[h] | 19.95 ± 4.05 | 0.042* |
| Urea before HD (mmol/L) | 27.48 ± 5.83[i] | 24.73 ± 5.93 | 23.78 ± 6.18[i] | 26.47 ± 4.34 | 0.039* |
| Albumins (g/L) | 37.63 ± 5.41[b] | 42.42 ± 4.67[b,j,k] | 37.13 ± 5.90[j] | 38.48 ± 4.74[k] | <0.001* |
| Total cholesterol (mmol/L) | 5.22 ± 0.88[j] | 5.22 ± 0.96[j] | 5.44 ± 0.87[b] | 4.38 ± 0.77[j,b] | <0.001* |
| LDL (mmol/L) | 3.30 ± 0.93[b] | 3.07 ± 0.98[b] | 3.40 ± 0.73[b] | 1.99 ± 0.60[b] | <0.001* |
| HDL (mmol/L) | 1.10 ± 0.34[b] | 1.28 ± 0.50[b,j] | 1.19 ± 0.22 | 1.71 ± 0.42[b,j] | <0.001* |
| Glucose (mmol/L) | 4.64 ± 0.98[l] | 5.59 ± 1.51[l,m] | 5.46 ± 1.36 | 4.60 ± 1.33[m] | 0.033* |
| Ultrafiltration per HD (L) | 3.58 ± 1.19[a,n] | 3.03 ± 1.30[a] | 2.86 ± 1.00[n] | 3.55 ± 1.20 | 0.037* |

*$P$ <0.05

Significance levels: [a]: $P$ = 0.032; [b]: $P$ <0.001; [c]: $P$ = 0.009; [d]: $P$ = 0.016; [e]: $P$ = 0.041; [f]: $P$ = 0.027; [g]: $P$ = 0.015; [h]: $P$ = 0.026; [i]: $P$ = 0.039; [j]: $P$ = 0.001; [k]: $P$ = 0.011; [l]: $P$ = 0.049; [m]: $P$ = 0.041; [n]: $P$ = 0.021

BP: blood pressure; HD: haemodialysis; HDL: high-density lipoproteins; LDL: low-density lipoproteins; Kt/V: single dialysis efficiency; MAP: mean arterial pressure

Table 3. Differences in Biochemical and Clinical Parameters Between Cold (March and December) and Mild (June and September) Months (Student's *t*-test for Independent's Data)

| | Cold months | Mild months | *P* |
|---|---|---|---|
| Number of HD | 67 | 68 | |
| Calcium (mmol/L) | 2.58 ± 0.25 | 2.57 ± 0.23 | 0.766 |
| Phosphorus (mmol/L) | 1.48 ± 0.47 | 1.72 ± 0.51 | 0.005* |
| Creatinine before HD (mmol/L) | 1.26 ± 0.29 | 1.26 ± 0.34 | 0.900 |
| Creatinine after HD (mmol/L) | 0.49 ± 0.15 | 0.51 ± 0.15 | 0.538 |
| Erythrocytes number (*$10^{12}$) | 3.41 ± 0.48 | 3.47 ± 0.46 | 0.448 |
| Haemoglobin (g/L) | 108.52 ± 13.43 | 112.09 ± 13.61 | 0.128 |
| Alkaline phosphatase (IU/L) | 119.46 ± 69.03 | 169.78 ± 107.98 | 0.002* |
| Aspartate aminotransferase (IU/L) | 10.23 ± 5.23 | 11.09 ± 10.06 | 0.534 |
| Alanine aminotransferase (IU/L) | 16.67 ± 5.41 | 18.76 ± 13.14 | 0.228 |
| Y-glutamyl transpeptidase (IU/L) | 21.71 ± 12.24 | 22.75 ± 23.36 | 0.747 |
| Urea before HD (mmol/L) | 27.13 ± 5.35 | 24.40 ± 5.99 | 0.006* |
| Urea after HD (mmol/L) | 10.19 ± 2.93 | 9.16 ± 3.08 | 0.051 |
| Total proteins (g/L) | 66.18 ± 5.01 | 67.40 ± 4.82 | 0.158 |
| Albumins (g/L) | 37.92 ± 5.17 | 40.58 ± 5.69 | 0.006* |
| Total cholesterol (mmol/L) | 4.93 ± 0.93 | 5.30 ± 0.93 | 0.023* |
| LDL (mmol/L) | 2.85 ± 1.04 | 3.23 ± 0.87 | 0.046* |
| HDL (mmol/L) | 1.30 ± 0.47 | 1.23 ± 0.39 | 0.399 |
| Triglycerides (mmol/L) | 2.21 ± 0.98 | 2.23 ± 0.89 | 0.936 |
| Glucose (mmol/L) | 4.62 ± 1.15 | 5.57 ± 1.46 | 0.004* |
| Leukocytes number (*$10^{9}$) | 6.44 ± 1.92 | 6.46 ± 1.89 | 0.951 |
| Systolic BP before HD (mmHg) | 145.93 ± 27.29 | 143.93 ± 26.70 | 0.668 |
| Diastolic BP before HD (mmHg) | 79.42 ± 15.52 | 79.40 ± 14.05 | 0.993 |
| Systolic BP after HD (mmHg) | 133.30 ± 26.21 | 134.88 ± 28.88 | 0.739 |
| Diastolic BP after HD (mmHg) | 74.18 ± 15.13 | 72.93 ± 13.60 | 0.614 |
| Body mass before HD (kg) | 75.41 ± 13.00 | 74.30 ± 13.26 | 0.624 |
| Body mass after HD (kg) | 72.24 ± 12.63 | 71.74 ± 12.53 | 0.818 |
| Ultrafiltration per HD (L) | 3.57 ± 1.18 | 2.97 ± 1.20 | 0.004* |
| Kt/V | 1.23 ± 0.25 | 1.22 ± 0.30 | 0.694 |
| MAP before HD (mmHg) | 101.59 ± 17.97 | 100.91 ± 17.15 | 0.822 |
| MAP after HD (mmHg) | 93.89 ± 17.25 | 93.58 ± 17.85 | 0.919 |

*$P$ <0.05

BP: blood pressure; HD: haemodialysis; HDL: high-density lipoproteins; Kt/V: single dialysis efficiency; LDL: low-density lipoproteins; MAP: mean arterial pressure

## Discussion

Seasonal variations in clinical and laboratory variables appear to be common in chronic haemodialysis patients, but previous detailed investigations have been conducted mostly among American chronic haemodialysis patients. We investigated the influence of seasons on clinical and biochemical parameters in a group of chronically haemodialysed patients living in a mild Mediterranean climate on the Adriatic coast in South Croatia, Europe. This is the first detailed European report of seasonal variations in clinical parameters in chronically haemodialysed patients. The study confirmed significant seasonal variations in the blood concentrations of phosphorus, pre/postdialysis creatinine, alkaline phosphatase, alanine aminotransferase, urea before HD, albumins, total cholesterol, LDL cholesterol, HDL cholesterol, glucose, and ultrafiltration per HD. Similar investigation based on the data from Haemodialysis (HEMO) study was conducted by Cheung et al[9] in 15 clinical centres in various parts of the USA. They found that seasonal variations in predialysis blood urea nitrogen concentrations peaked in March, which coincided approximately with peak protein catabolic rates, as well as protein and energy intakes (determined by dietary recall). Furthermore, the same report[9] described that total ultrafiltration volume and predialysis weight were lowest in the summer and these variables both correlated with outdoor temperature. In the same study,[9] haematocrit also varied with the seasons and the mean predialysis haematocrit values were highest in July, which could not be attributed solely to the estimated changes in plasma volume. In our study, we demonstrated the same pattern of lower predialysis blood urea concentration in summer, which could be attributed to a decrease in food intake. We also demonstrated a lower ultrafiltration rate during warmer months. This might be attributed to insufficient ingestion (due to loss of appetite) and greater sweating during the warm and humid Mediterranean summer. We could not demonstrate seasonal

variations in haemoglobin concentration. On the contrary, in warmer months we demonstrated higher blood concentrations of albumins, total cholesterol, LDL cholesterol, and glucose, which obviously could not be attributed just to seasonal differences in food intake. We speculate that some hormonal influences could be involved in those observations. Thang et al[10] demonstrated that parathyroid hormone levels in chronically haemodialysed patients increased markedly in the summer, but this might be attributed to the insufficient ingestion of calcium, vitamins, and other nutrients due to loss of appetite. We unveiled lower concentrations of phosphorus and alkaline phosphatase during the colder months and these observations should not be attributed to dietary intake.

Despite the fact that certain laboratory variables of chronic haemodialysis patients vary with the seasons, most of the previous investigations focused on blood pressure variations. Our study could not confirm significant seasonal differences in any of the measured blood pressure parameters. Argiles et al[6] demonstrated that in patients with end-stage renal disease treated with haemodialysis, blood pressure varies seasonally, with higher values in the winter and lower values in the summer. Tozawa et al[11] found that ambient temperature and relative humidity correlated strongly with blood pressure and body weight in dialysed patients. Sposito et al[12] found seasonal variations of blood pressure in dialysis patients that were associated and synchronous with seasonal changes in chronic overhydration status. Both cycles depended on conditions influenced by the annual daylight span more than by external temperature. On the contrary, Fine[13] demonstrated that season had no effect on blood pressure in haemodialysis patients in a North American centre. He concluded that reported seasonal changes in blood pressure in Europe might be related to non-climatic factors. For example, Argiles et al[14] suggested that seasonal differences in vitamin D3 blood levels is one of the factors which result in the seasonal variation of blood pressure in dialysis patients. Consequently, reported seasonal differences in blood pressure parameters in dialysed populations might be the result of a combination of factors, including extracellular volume overload, ambient temperature and humidity, hormonal influences and levels of autonomic nerve system activity. Iseki et al[15] showed a strong correlation between ambient temperature and the incidence of end-stage renal disease. Uremic symptoms leading to initiate dialysis, such as congestive heart failure, may be aggravated in lower ambient temperatures, due to the inverse relationship between ambient temperature and sympathetic nerve function. We could not demonstrate blood pressure seasonal differences in chronically dialysed patients in a Mediterranean climate and this observation might be partly due to weak summer-winter changes in ambient temperature.

In summary, in Mediterranean climates, seasonal differences in predialysis urea concentration and ultrafiltration rate per dialysis can be attributed to different food and water intake. The demonstrated seasonal differences in blood concentration of phosphorus, alkaline phosphatase, total cholesterol, LDL cholesterol, and glucose must be the result of neurohormonal influences and cannot be imputed to ingestion variations. This climate has no impact on haemoglobin concentration and blood pressure, despite previous reports which have described such seasonal variations. The major weakness of this paper is the failure to control for dietary intake; consequently, observed results remain speculative.

Failure to consider all these variations might lead to biases in the interpretation of clinical studies. Conversely, the biases could also be the consequences of constant clinical data misinterpretations, based on expectations of the seasonal variations of such data. In addition, awareness of all these results might facilitate the interpretation of laboratory results and the treatment of these patients.

Based on the results of this investigation conducted on chronically haemodialysed patients in a mild Mediterranean climate in South Croatia, we conclude that clinicians should pay attention to seasonal factors when interpreting biochemical analyses or prescribing medication and dialysis parameters. Further investigation should be conducted in different continents encompassing both hemispheres, especially in climates with greater seasonal differences in ambient temperature and relative humidity.

REFERENCES

1. Shahar DR, Froom P, Harari G, Yerushalmi N, Lubin F, Kristal-Boneh E. Changes in dietary intake account for seasonal changes in cardiovascular disease risk factors. Eur J Clin Nutr 1999;53:395-400.
2. Goran MI, Nagy TR, Gower BA, Mazariegos M, Solomons N, Hood V, et al. Influence of sex, seasonality, ethnicity, and geographic location on the components of total energy expenditure in young children: implications for energy requirements. Am J Clin Nutr 1998;68:675-82.
3. Magnusson A. An overview of epidemiological studies on seasonal affective disorder. Acta Psychiatr Scand 2000;101:176-84.
4. Moshkowitz M, Konikoff FM, Arber N, Peled Y, Santo M, Bujanover Y, et al. Seasonal variation in the frequency of Helicobacter pylori infection: a possible cause of the seasonal occurrence of peptic ulcer disease. Am J Gastroenterol 1994;89:731-3.
5. Boulay F, Berthier F, Sisteron O, Gendreike Y, Gibelin P. Seasonal variation in chronic heart failure hospitalizations and mortality in France. Circulation 1999;100:280-6.
6. Argiles A, Mourad G, Mion C. Seasonal changes in blood pressure in patients with end-stage renal disease treated with hemodialysis. N Engl J Med 1998;5:1364-70.
7. Daugirdas JT. Second generation logarithmic estimates of single-pool variable volume Kt/V: an analysis of error. J Am Soc Nephrol 1993,4: 1205-13.

8. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499-502.
9. Cheung AK, Yan G, Greene T, Daugirdas JT, Dwyer JT, Levin NW, et al. Seasonal variations in clinical and laboratory variables among chronic hemodialysis patients. J Am Soc Nephrol 2002;13:2345-52.
10. Thang NT, Yamaguchi O, Yoshimura Y, Shiraiwa Y, Kumagai I. Seasonal changes of parathyroid hormone in chronic hemodialysis patients. Fukushima J Med Sci 1993;39:29-33.
11. Tozawa M, Iseki K, Iseki C, Morita O, Yoshi S, Fukiyama K. Seasonal blood pressure and body weight variation in patients on chronic hemodialysis. Am J Nephrol 1999;19:660-7.
12. Sposito M, Nieto FJ, Ventura JE. Seasonal variations of blood pressure and overhydration in patients on chronic hemodialysis. Am J Kidney Dis 2000;35:812-8.
13. Fine A. Lack of seasonal variation in blood pressure in patients on hemodialysis in a North American center. Am J Kidney Dis 2000;36: 562-5.
14. Argiles A, Lorho R, Servel MF, Couret I, Chong G, Mourad G. Blood pressure is correlated with vitamin d(3) serum levels in dialysis patients. Blood Purif 2002;20:370-5.
15. Iseki K, Morita O, Fukiyama K. Seasonal variation in the incidence of end-stage renal disease. Am J Nephrol 1996;16:375-81.