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Mortality in Hemodialysis Patients Over 65 Years of Age

Aida Coric[1], Halima Resic[1], Damir Celik[2], Fahrudin Masnic[1], Selma Ajanovic[1], Nejra Prohic[1], Amela Beciragic[1], Emir Grosa[1], Ajdin Smajlovic[1], Aida Mujakovic[3]

[1]Clinic of Hemodialysis, University Clinical Centre, Sarajevo, Bosnia and Herzegovina
[2]Clinic of Physical Medicine and Rehabilitation, University Clinical Centre, Sarajevo, Bosnia and Herzegovina
[3]Department of Internal Medicine, General Hospital „Prim. dr Abdulah Nakas“, Sarajevo, Bosnia and Herzegovina

Corresponding author: Aida Coric, MD, MS. Clinic of Hemodialysis, University Clinical Centre, Bolnička 25, 71000 Sarajevo, Bosnia and Herzegovina, Tel: + 387 33 298 230. E-mail: idacoric@yahoo.com

ABSTRACT

Introduction: Based on the statistics the population in Bosnia and Herzegovina is getting older. In 2013 the average life span for women was 73.6 years and 68.1 for men. The chronic hemodialysis program is mainly reserved for elderly patients with high mortality risk. The most common cause of hemodialysis mortality relates to cardiovascular diseases (60.2%), regardless of frequent innovations and improvement of hemodialysis procedures. **The aim of the study** was to determine the mortality rate by age groups with comments on the presence of non-traditional predictors (anemia, hypoalbuminemia, CRP, vascular access and PTH) in dialysis patients in the follow-up period of 36 months. **Methods:** The study included all patients undergoing chronic hemodialysis treatment at the Clinic of Hemodialysis of the Clinical Center University of Sarajevo (CCUS). **Results:** Out of a total number of hemodialysis patients *(n=232),* the specific mortality rate in patients under 65 years of age was 16.8%, and 50.5% in patients over 65 years of age. According to the age groups the mortality rate in elderly patients is as follows: from 65 to 74 years (45.1%), from 75 to 84 years (55.0%), over ≥85 years (75.0%). The most frequent vascular access in patients under and above 65 is arteriovenous fistula (79.6% and 62.1 %), temporary hemodialysis catheter (11.7% and 43.8 %) and long-term hemodialysis catheter (8.8% and 4.2 %). In the age group under 65 years of age the temporary hemodialysis catheter is significantly and more frequently used in diseased patients in respect to survivors (34.8% vs. 7.0%) [$\chi^2(2)=15.769$, p=0.001]. Diseased patients from the age group over 65 had a significantly lower mean value of haemoglobin in blood (M=100.9±17.5 g/L) in respect to survivors (M=109.2±17.1)[t(93)=2.339; p=0.021], lower mean value of albumin in blood (Me=32.0; IQR=29.0 do 35.0) in respect to survivors (Me=34.0; IQR=32.0 to 38.0) [U=762.5; p=0.006], and higher mean value of CRP in blood (Me=19.3 mg/L; IQR=6.6 to 52.0) in respect to survivors (Me=7.8; IQR=4.0 to 16.7) [U=773.5; p=0.008]. Diseased patients belonging to the age group over 65 had lower mean value of PTH, but without statistical significance (p>0.05). **Conclusion:** older age, temporary vascular access, anaemia and hypoalbuminemia are strong predictors of mortality in hemodialysis patients. Old age does not present contraindication for hemodialysis treatment, and treatment of terminal renal illness should not be abandoned.

Key words: hemodialysis, mortality, old age.

1. INTRODUCTION

According to the Agency for Statistics of BiH, the population is getting older and the warning of demographers that life expectancy in BiH is gradually increasing are grounded, but indicators also reveal that the lifespan of the BiH citizens is constantly increasing. Last year, the average life expectancy for women was 73.6 years and 68.1 for men. Twelve years ago the average life expectancy of women in Bosnia and Herzegovina was 69.2 years, while men on average died at the age of 63.3. It is obvious that in this not-so-large period the life expectancy of women in BiH increased by 4.4 years and by 4.8 for men. In Bosnia and Herzegovina, the average life expectancy is 74.9 years where, according to the latest UN statistics, the average life expectancy for men was 72.2 years and 77.4 for women. Based on the age data, it follows that mainly elderly people are ill and included in the chronic hemodialysis treatment, and that cardiovascular diseases (60.2%) are the most common cause of mortality in hemodialysis, regardless of more frequent innovations and trainings in the dialysis procedures (1). Over 50% of the total number of deaths on hemodialysis (HD) relate to cardiovascular causes (2, 3). Cardiovascular mortality in hemodialysis population is about 9% per year, and the most important complications include left ventricular hypertrophy, congestive heart failure and ischemic heart disease (2, 3, 4, 5). Despite technological progress of hemodialysis and application of different dialysis techniques, in addition to timely start of he-

modialysis treatment, morbidity and mortality in the five-year survival on hemodialysis is still high (2, 6). The pathogenesis of cardiovascular damage in chronic renal disease is more complex in comparison to other, general population. Old age and presence of comorbidity, as well as poor social life conditions are also important in the prognosis and outcome of cardiovascular diseases. For monitoring mortality it is of great importance from the very beginning of the hemodialysis treatment to monitor the percentage of the so called non-traditional risk factors for cardiovascular disease. For decades it has been known that hypertension, diabetes mellitus, hyperlipidemia, obesity, smoking, and low physical activity/inactivity affect the occurrence of cardiovascular diseases and present the traditional risk factors (2, 7). In hemodialysis population "non-traditional" factors are significant predictors of cardiovascular disease. Non-traditional risk factors are divided in two groups:

Hemodynamic factors (anemia, hypervolemia, AV fistula with flow QAV> 1000 ml / min). Metabolic factors (hypoalbuminemia, hyperhomocysteinemia, micro inflammatory, secondary hyperparathyroidism, oxidative stress) (2, 7).

2. AIM

The aim of the study was to determine the mortality rate by age groups with comments on the presence of non-traditional predictors (anemia, hypoalbuminemia, CRP, vascular access and PTH) in dialysis patients.

3. PATIENTS AND METHODS

The prospective clinical study included all patients undergoing chronic hemodialysis treatment at the Clinic of Hemodialysis of the Clinical Center University of Sarajevo (total number of hemodialysis patients was 232). Follow-up period was 36 months (from December 2011 to December 2014).

At all patients were analyzed data from medical records: age, gender, mean age, underlying disease, vascular access, hemoglobin, albumin, CRP, PTH. Also we detected the date of death. All blood tests were analyzed at the Institute for Clinical Chemistry and Biochemistry with standard methods, four times per year in the follow-up period of three years. CBC and hemoglobin were measured using impedance and optical method: counter, Abbott CELL DYN 3700 and SIEMENS ADVIA 2120. Serum albumin levels were determined by spectrophotometry standard bromcresol green method (BCG). C reactive protein (CRP) are quantitatively determined using the apparatus immunonephelometric Dimension system, Dade Behring.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 21.0 for Windows system (SPSSInc., Chicago, Illinois, USA). Data is presented as mean ± standard deviation or as median with interquartile range (IQR, 25th to 75th percentiles) dependent on normality of variables distribution. The Kolmogorov–Smirnov statistic with a Lilliefors significance level was used for testing normality of distibution. In the case of categorical variables, counts and percentages were reported. The chi-square test is used for categorical data. Differences between groups were tested using the parametric Independent Sampled t-test and non-parametric Mann Whitney U test. Case-Fatality Rate (percent) was calculated according to the formulas: number of individuals dying during a specified period of time after disease onset or diagnosis / number of individuals with the specified disease x 100. All statistical tests were two-sided, and p-value less than 0.05 was considered as significant.

4. RESULTS

Out of 232 patients, 137 (59.1%) were males and 95 (40,9 %) females. The median age for females was 64.0 years (IQR=56.0 to 73.0) and 59.0 (IQR=49.0 to 69.5) for males. The case-fatality rate in the three year period was 30.6%. Patients over ≥ 65 years had a significantly (*p<0.001*) higher case-fatality rate than younger patients, 50.5% versus 16.8%; the relative risk was 3.01 (95% confidence interval (CI): 1.97, 4.59) (Figure 1).

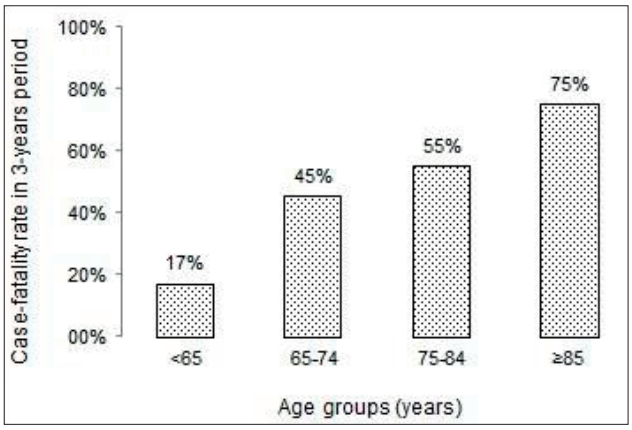

Figure 1. The case-fatality rate in hemodyalisis patients in three years period

In patients over ≥ 65 years, more frequent etiological factors for end-stage renal disease were as follows: diabetes mellitus type 2 (27.4%), other causes (22.1%), nephritis chronica (18.9%), nephroangiosclerosis (16.8%), polycystic kidney disease (8.4%) glomerulonephritis chronica (5.3%), and diabetes mellitus type 1 (1.1%). In patients under <65 years, more frequent etiological factors for end-stage renal disease were: nephritis chronica (23.4%), other causes (22.6%), glomerulonephritis chronica (18.2%), nephroangiosclerosis (13.1%), diabetes mellitus type 2 (11.7%), polycystic kidney disease (8.0%) and diabetes mellitus type 1 (2.9%). Diabetes mellitus type 2 is statistically significantly more frequent in elderly patients, and glomerulonephritis chronica in younger patients [$\chi^2(6)= 16.889$; $P = 0.01$]. In patients over ≥ 65 years, more frequent vascular access was: arteriovenous fistula (62.1%), venous catheter (43.8%) and long-term venous catheter (4.2%). In younger patients, more frequent vascular access was: arteriovenous fistula (79.6%), venous catheter (11.7%) and long-term venous catheter (8.8%).

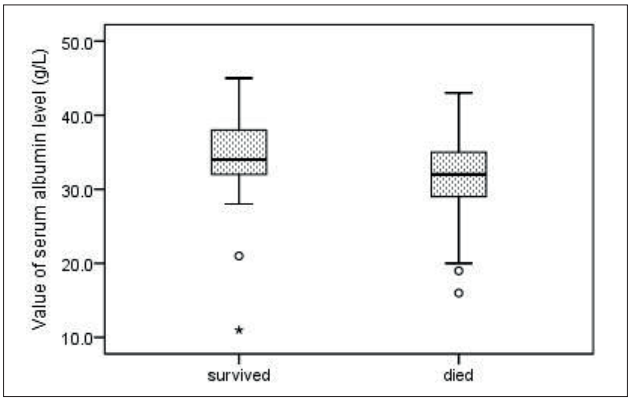

Figure 2. Significant lower median values of serum albumin level in diseased hemodyalisis patients as compared to survivors (p <0.01)

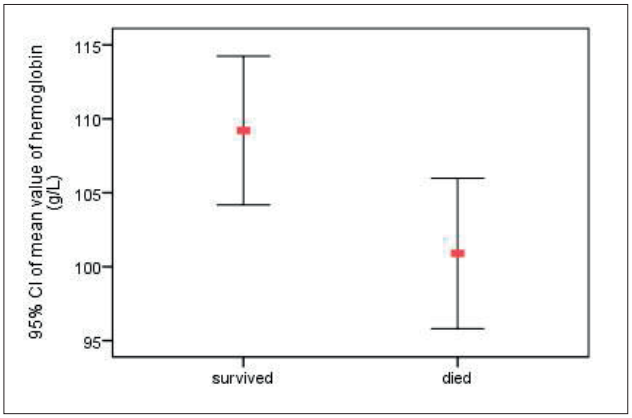

Figure 3. Significant lower mean hemoblobin values in diseased hemodyalisis patients as compared to survivors (p <0.05)

There was a significant association between the vascular access and lethal outcomes [$\chi^2(2) = 27.596$; *p <0.001*]. This seemingly refers to the fact that, based on odds ratio, the odds of lethal outcomes were 5.16 times higher if they had a venous catheter than if they had arteriovenous fistula or a long-term catheter.

In the age group ≥65 years, deceased patients had: lower mean value of hemoglobin in serum (g/L) (M = 100.9 ± 17.5) compared to survivors (M = 109.2 ± 17.1) [t(93) = 2.339; *p = 0.021*]; lower median of serum albumin values (g/L) (Me = 32.0; IQR = 29.0 to 35.0) compared to survivors (Me=34.0; IQR=32.0 do 38.0) [U=762.5; p=0.006]; and higher values of C-reactive Protein in serum (mg/L) (Me = 19.3; IQR = 6.6 to 52.0) compared to survivors (Me = 7.8; IQR = 4.0 to 16.0) [U = 773.5; *p = 0.008*)].

Patients with lethal outcomes had a lower median of parathyroid hormone value (pg/mL), in patients ≥ 65 years and < 65 years, but the differences were not significant *(p >0.05).*

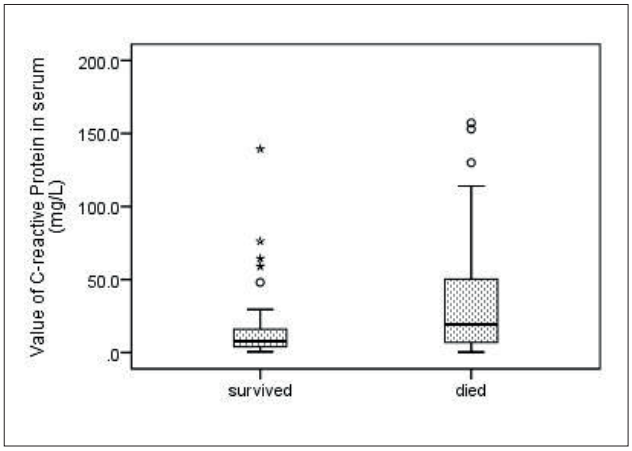

Figure 4. Significant higher values of CRP median values in serum of diseased hemodyalisis patients as compared to survivors (p <0.01)

5. DISCUSSION

The specific mortality rate in the population under <65 years of age was 16.8% (23/137), the mortality rate in the population over ≥65 years was 50.5%. Mortality rate by age groups in the population over ≥ 65 years was 45.1% or 23/51, from 65-74 years 55.0% or 22/40, 75-84 years and ≥85 years 75.0%. Causes of death in elderly patients on dialysis did not differ significantly from those in younger patients, and the two largest groups related to cardio-vascular diseases and infections. Fatal infections are probably more common in elderly patients due to altered immune status, although there is little direct evidence in that regard.

There is a statistically significant association between temporary catheters as a vascular access, and death, respectively. In the group under <65 years of age temporary catheter is used significantly more often in diseased patients as compared to survivors (34.8% vs. 7.0%; p=0.001). Deceased patients in the group over > 65 years of age had significantly lower values of hemoglobin and albumin, as major non-traditional predictors of dialysis patient mortality.

Anemia is a significant cause of the left ventricular hypertrophy. Over 90% of patients treated with hemodialysis suffer from chronic anemia. Decrease in hemoglobin of 10 g/L in hemodialysis patients is associated with an increase of 10 g/m^2 in the left ventricular myocardium (2, 3, 8, 9). We can not ignore the fact that when starting the hemodialysis treatment patients already suffer from several months and even a year chronic anaemia. It is important to achieve targeted Hb values of 100-120 g/l (mean Hb = 110); Hct (33-36%); ferritin level of 200-500 ng/ml, by daily administration of erythropoietin and iron (3, 9, 10, 11). Patients with a healthier cardio-vascular system are generally more suitable for the hemodialysis treatment. In all patients, the hemoglobin values should be maintained in the range from 100 to 120 g/L.

Hypoalbuminemia with inflammation and the MIA syndrome development (malnutrition, inflammation, atherosclerosis) present a high risk of mortality in HD. The albumin concentration below 35 g/L, and in particular the concentration below 30 g/L is defined by malnutrition component and low level blood cholesterol. These results indicate that old age, temporary vascular access, anemia and hypoalbuminemia are strong mortality predictors in dialysis patients.

Secondary hyperparathyroidism is often present in dialysis patients and is associated with impaired cardiac function and left ventricular hypertrophy (3, 7). Increased concentrations of serum phosphate (PO 4> 2.1 mmol / L), increased product of Ca x PO 4> 5.65 mmol / L and increased PTH concentration (iPTH> 500 pg/ml) significantly increase the risk of mortality in HD. A dietary regime, "binder phosphorus" and active Vitamin D metabolite should provide optimal phosphate concentration <1.6 mmol/L, product of Ca x PO 4 <4.4 mmol/L and concentration of iPTH 100-200 pg/mL, although according to the American KDOQI guideline for HD (hyperparathyroidism) PTH values are in the referenced values of 150-300 pg/mL for patients included in the chronic hemodialysis treatment (3, 10).

Inflammation (CRP> 10 mg/L) is present in > 30% of patients on hemodialysis. Interleukin 6, as an inflammation factor with CRP, is a major risk factor. The use of aspirin, statin preparations, significantly reduces the concentration of proinflammatory cytokines. Bicarbonate HD with the use of a dialyzer with biocompatible membranes and high-flux dialyzers (high-throughput membrane) ultrapure water, and the endotoxin concentration, which must be below <5 pg/mL or 0.03 EU/mL, significantly contributes to the reduction of CRP (12, 13, 14).

Elderly patients are more slowly adapting to the dialysis regime, they are more sensitive to changes in the volume of body fluids, spend more time in hospitals, have a higher mortality due to infections and cardiovascular disease, and inevitably shorter survival time as compared to younger patients (15,16). In 75

year old patients dialysis increases the mortality risk of death for less than three times, whereas the same risk at the age of 45 is even 20 times higher than expected for that age (15, 16, 17).

6. CONCLUSION

Old age does not present contraindication for hemodialysis treatment, and treatment of terminal renal illness should not be abandoned. In recent decades elderly patients with chronic renal failure were seldom candidates for renal replacement therapy mainly due to the lack of places in hemodialysis centers in 1960s and 1970s of the last century. The majority of doctors considered that elderly patients could not stand the hemodialysis treatment. This negative opinion regarding the dialysis treatment of elderly patients has been changed in almost all industrial developed countries. However, the opinions differ in undeveloped and in developing countries, and it is not uncommon that the dialysis treatment, and especially kidney transplants are not available to elderly patients.

CONFLICT OF INTEREST: NONE DECLARED.

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