**Low Glomerular Filtration Rate is Not Associated With Comorbidities and Reasons For Hospitalization İn Geriatric Patients Over 75 Years Of Age**

Hatice Hamarat

Departmen of Internal Medicine , 26080,Turkey

 contribution of all authors to the work: There is only one author contributing to the article. All contributions to the article belong to a single author.

**Corresponding author name**:

MD Hatice HAMARAT, Internal Medicine Department, 71 Evler Mahallesi,Çavdarlar Sokak ,26080,Eskişehir City Hospital, Eskişehir,Turkey.

including zip code: 26080

hklncal@hotmail.com

ABSTRACT

Background: With an increase in the elderly population, the frequency of hospitalizations in recent years has also risen at a rapid pace. This, in turn, has resulted in poor outcomes and costly treatments. Hospitalization rates increase in elderly patients due to a decline in glomerular filtration rate (GFR). This study aimed to investigate the connection between GFR and and comorbidity and reasons for hospitalization in elderly patients. Methods: We analyzed patients aged 75 years and over who were admitted to the internal medicine clinic of a tertiary hospital in Eskisehir. At admission, we calculated GFR values using the Modification of Diet in Renal Disease study (MDRD) formula and classified them into six categories: G1, G2, G3a, G3b, G4, and G5. We analyzed associations with hospitalization diagnoses and comorbidity factors. Results: The average age of the patients was 80.8 years (±4.5). GFR was 57.287±29.5 mL/kg/ 1.73 m2 in women and 61.3±31.5 mL/kg/ 1.73 m2 in men (p=0.106). Most patients were admitted to the hospital at the G2 stage (32.8%). The main reasons for hospitalization were anemia (34.4%, 28.6%) and malnutrition (20.9%, 20.8%) in women and men, respectively. The most frequent comorbidity leading to hospitalization was arterial hypertension (n=168, 28%), followed by diabetes (n=166, 27.7%). Conclusion: When evaluating geriatric patients, low GFR alone does not provide sufficient information. Patients' comorbid factors should also be taken into account. There is no association between low GFR during hospitalization and hospitalization-related diagnoses.

Keywords: Aging, Glomerular Fıltratıon Rate, Hospıtalızatıon, Comorbidity.

INTRODUCTION

As an individual ages, there arises a noticeable decrease in GFR, which reflects the loss of renal function. It becomes difficult to differentiate between GFR loss due to healthy aging and a decline caused by renal diseases.1 As a result, using GFR measurements to determine prognosis in older adults becomes problematic. As a consequence of the anticipated reduction in GFR of 1 mL/min/1.73 m² per year, healthy older adults exhibit a reduced eGFR in comparison to younger adults. 2-4 Research showed that 50% of people aged over 70 years had a measured or estimated GFR lower than 60 mL/min/1.73 m².5 Furthermore, studies indicate a link between poor health outcomes and reduced GFR in patients with comorbidities.6 A population-based study recently reported the association between GFR loss and mortality.7 Multiple studies conducted in different countries with large patient populations have concluded that GFR loss raises the risk of mortality. 8-10

The appropriate management of renal failure is crucial in elderly patients, given its increasing prevalence, poor outcomes, and high treatment costs that contribute to a global public health issue. Our study aimed to explore the correlation between hospitalization diagnoses and GFR.

**METHODS**

**Participants aged 75 years and older who were regularly examined in internal medicine outpatient clinics were included in the study. Data from 600 patients were analyzed retrospectively. Individuals with indications for intensive care unit hospitalization and emergency hemodialysis were excluded. Only patients hospitalized in internal medicine clinics were included in the study. Age, gender, comorbidities, GFR, certain laboratory characteristics and hospitalization diagnosis were recorded. BMI was calculated according to the World Health Organization (WHO) guidelines.11 Hospitalization GFR values were calculated using the MDRD Study formula.12 Staging was based on six GFR categories: G1, G2, G3a, G3b, G4, and G5.13 GFR groups based on ml/min per 1.73 m2 were as follows: G1 with GFR ≥90, G2 with GFR 60-89, G3a with GFR 45-59, G3b with GFR 30-44, G4 with GFR 15-29, and G5 with GFR <15.**

**Statistical analysis**

**Mean and standard deviation were used to express continuous variables, and categorical variables were expressed as percentages. The obtained results were expressed using standard average and deviation. The Kolmogorov-Smirnov test was used to assess normality. The Pearson chi-square test was used to compare categorical parameters. The comparison of different numerical parameters was analyzed using an independent samples test. To evaluate the differences between groups, Fisher's exact test and ANOVA were used. For post-hoc analysis, Tucey and Tamhane were used. A p-value of less than 0.05 was considered statistically significant. The analysis was carried out using IBM SPSS Statistics 25 software.**

**RESULTS**

We examined 600 patients admitted to the internal medicine ward. Among them, 231 (38.5%) patients were male, and 369 (61.5%) were female. The difference between the numbers of male and female patients was not statistically significant (p=0.130). The average age of all patients was 80.8 (±4.5) years. The GFR was 57.287±29.5 mL/kg/ 1.73 m2 in women and 61.3±31.5 mL/kg/ 1.73 m2 in men (p=0.106). The GFR values of the patients during hospitalization were calculated using the MDRD formula and analyzed in six groups. The most common hospitalization stage for patients was G2 (32.8%). A total of 147 (24.5%) patients did not have any comorbidities. Arterial hypertension (n=168, 28%) was the most frequent comorbidity, followed by diabetes (n=166, 27.7%). Table 1 shows the characteristics of patients according to GFR groups.

Table 2 shows the analysis of patient diagnoses upon admission to the clinic according to GFR groups. There was no significant difference in hospitalization diagnoses between male and female patients (p=0.308). The primary reasons for hospitalization were anemia (34.4%, 28.6%) and malnutrition (20.9%, 20.8%) for women and men, respectively. Men had higher rates of hospitalization caused by pneumonia (5.2%) and acute renal failure (13.4%). Women had a higher incidence of urinary infections (8.4%). There was no statistically significant difference in comorbidities observed between men and women (p=0.078).The highest number of hospitalizations was observed among patients without comorbidities and those with diabetes and arterial hypertension. Table 3 illustrates the relationship between comorbidities and indications for hospitalization. The most common indications for hospitalization among patients without comorbidities were the G2 stage (43.5%), anemia (46.9%), and malnutrition (25.2%). Patients with Alzheimer's disease were admitted to hospitals in the G1 stage (40%), the common reason being malnutrition (40.9%). Patients with cerebrovascular occlusion were admitted to hospitals in the G5 stage (40%), with acute renal failure (40%) being the most frequent cause, followed by urinary infection (30%). Patients with COAD were hospitalized with anemia (50%) in the G3a stage (37.5%). Patients with cancer were hospitalized with anemia (45.5%) in the G3b stage (54.5%).

DISCUSSION

Approximately 50% of individuals over the age of 75 meet the present diagnostic criteria for chronic kidney disease (CKD). Yet, marking them all as ill is debatable.14 A lack of an exact definition of the standard GFR range for the elderly results in over diagnosing renal failure in the elderly population.15-17 Categorization of elderly patients with age-dependent e GFR decrease as chronic kidney disease is crucial, as it increases the likelihood of unwarranted intervention with extra implications for healthcare practices and policies for most of this age group.15-17 The GFR value of the patients in our study was 58.87 ± 30 mL/kg/ 1. 73 m² at the time of hospitalization (p < 0.001). We also found that patients with (32.8%) and without (43.5%) comorbidities were most commonly hospitalized in G2 stage. This indicates that comorbid factors did not affect the GFR values of the hospitalized patients.

In mortality studies in the elderly, low GFR has been evaluated as an important parameter.6 This study does not investigate mortality. GFR-related hospitalization diagnostics were not affected by the presence of comorbid factors. There was no significant difference in comorbidities between men and women (p=0.078). Of the hospitalized patients, 147 (24.5%) had no comorbidities. Diabetes (n=166, 27.7%) and arterial hypertension (n=168, 28%) were more prevalent. Our study found a significant difference only between patients without comorbidities (67.4±27.4 mL/kg/ 1.73 m²) and those with diabetes (53.5±28.3 mL/kg/ 1.73 m²) (p=0.001) and cancer (41.6±18.6 mL/kg/ 1.73 m²) (p=0.03). This difference can be attributed to the high frequency of diabetes in our study population and the low frequency of cancer patients. Hospitalization of cancer patients occurred at the G3b stage (54.5%), while diabetes patients were hospitalized at the G2 stage (25.9%).

Our study discovered that GFR values during hospitalization had no impact on the clinical diagnosis of hospitalization in the population over 75 years of age. Anemia and malnutrition were the most frequent hospitalization diagnoses across all GFR stages. Among women and men, anemia (34.4% and 28.6%, respectively) and malnutrition (20.9% and 20.8%, respectively) were the most common causes of hospitalization. The hospitalization diagnoses of male and female patients did not show a notable difference (p=0.308). The similar hospitalization diagnoses in all patients were attributed to gastrointestinal system absorption and function disorders that developed due to their advanced age and were independent of comorbid factors. This is why diagnoses of anemia and malnutrition were common. Earlier studies focused primarily on the relationship between low GFR, mortality, and comorbid factors. Mortality was found to increase as GFR decreased.18-20

In conclusion, the natural process of aging, coupled with a lack of effective healthcare policies, reduces the standard of living for senior citizens. If preventive medicine is not administered to healthy elderly individuals, they are more likely to require hospitalization. Renal dysfunction is one of the most critical problems associated with aging. Our study aims to highlight the physiologically low GFR in the elderly rather than focusing on the mortality rate. Therefore, we assessed GFR based on various stages. The hospitalization diagnoses were similar in individuals with all stages of GFR. The presence of comorbidities did not affect GFR during hospitalization, according to our findings. We anticipate that our findings will add to the existing literature since we did not come across a study that was akin to ours. Our study indicates that the GFR at the time of diagnosis correlates with the age of the patient and the aging of the kidney. Special GFR calculations should be made for patients aged 75 years and older, using distinct formulas not currently available. These calculations should take into account the physiological aging process of the kidney.

**STUDY LİMİTATİONS**

The GFR value of patients in the study was determined using a single method. While there are several alternative methods to measure GFR and compare the value during hospitalization with that from 6 months prior, unavailable pre-hospitalization examinations limited our scope. Future studies should consider measuring GFR using various methods across larger population samples in narrower age ranges.

**Authors’ contributions**

Single author: The author contributed solely to the article.

**Availability of data and materials**

The data belongs to a hospital and cannot be shared.

**Financial support and sponsorship**

None.

**Conflicts of Interest**

The authors have no potential conflicts of interest to disclose.

**Ethical approval and consent to participate**

The study received approval from the relevant Institutional Review Board based on decision E-25403353-050.99-2020 and assigned number 307.

**Consent for publication**

Not applicable

**REFERENCES**

1.Noronha IL, Santa-Catharina GP, Andrade L, Coelho VA, Jacob-Filho W,Elias RM. Glomerular filtration in the aging population. Front Med (Lausanne) 2022; 15;9:769329.

2.Eriksen BO, Palsson R, Ebert N, Van Der Giet M, Gudnason V Olafur, S Indridason et. al. GFR in healthy aging: an individual participant data meta-analysis of iohexol clearance in European population-based cohorts. J Am Soc Nephrol 2020;31(7):1602-1615.

3. Glassock RJ, Rule AD. Aging and the kidneys: anatomy, physiology and consequences for defining chronic kidney disease. Nephron 2016;134(1):25-29.

4. Schmitt R, Melk A. Molecular mechanisms of renal aging. Kidney Int 2017;92(3):569-579.

5. Ebert N, Jakob O, Gaedeke J, Giet VD. Prevalence of reduced kidney function and albuminuria in older adults: The Berlin initiative study. Nephrol Dial Transplant (2017) 32:997–1005.

6.Fravel MA, Ernst ME, Webb KL, Wetmore JB, Wolfe R, Woods RL et.al. Aspirin in Reducing Events in the Elderly Investigator Group. GFR Variability, Survival, and Cardiovascular Events in Older Adults. Kidney Med 2022, 5(2):100583.

7. Wu J, Jia J, Li Z, Pan H, Wang A, Guo X et.al. Association of estimated glomerular filtration rate and proteinuria with all-cause mortality in community-based population in China: a result from Kailuan study. Sci Rep 2018;8:2157.

8. Fung CS, Wan EY, Chan AK, Lam CL. Association of estimated glomerular filtration rate and urine albumin-to-creatinine ratio with incidence of cardiovascular diseases and mortality in chinese patients with type 2 diabetes mellitus - a population-based retrospective cohort study. BMCnephrology 2017; 18(1):47.

9. Wan EYF, Fong DYT, Fung CSC, Yu EYT, Chin WY, Chan AKC et.al. Prediction of five-year all-cause mortality in Chinese patients with type 2 diabetes mellitus - A population-based retrospective cohort study. Journal of diabetes and its complications 2017; 31(6):939-944.

10. Park M, Yoon E, Lim YH, Kim H, Choi J, Yoon HJ. Renal hyperfiltration as a novel marker of all-cause mortality. Journal of the American Society of Nephrology: JASN 2015 ;26(6):1426-33.

 11.WHO Consultation on Obesity World Health Organization. Obesity: preventing and managing the global epidemic: report of a WHO consultation. 2023. Available: https:// apps.who.int/iris/handle/10665/42330.

12. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. modification of diet in renal disease study group. Ann Intern Med 1999;130:461–70.

13. Delanaye P, Schaeffner E, Ebert N, Mariat C, Krzesinski JM, Moranne O. Normal reference values for glomerular filtration rate: What do we really know? Nephrol Dial Transplan 27(7):2664-72.

14. Ellam T, Twohig H, Khwaja A. Chronic kidney disease in elderly people: disease or disease label? BMJ 2016;352:h6559.

 15. O'Hare AM, Rodriguez RA, Rule AD. Overdiagnosis of chronic kidney disease in older adults—an inconvenient truth. JAMA Intern Med 2021; 181(10):1366-1368.

16. Winearls CG, Glassock RJ. Classification of chronic kidney disease in the elderly: pitfalls and errors. Nephron Clin Pract 2011;119(1):c2-4.

17. Liu P, Quinn RR, Lam NN, Elliott MJ, Xu Y, James MT et.al. Accounting for age in the definition of chronic kidney disease. JAMA Intern Med 2021;181:1359–66.

18. Warnock DG, Delanaye P, Glassock, RJ. Risks for All-Cause Mortality: Stratified by Age, Estimated Glomerular Filtration Rate and Albuminuria. Nephron 2017; 136:292–297.

19. Chen YT, Shih CJ, Ou SM, Hung SC, Lin CH, Tarng GC. Periodontal Disease and Risks of Kidney Function Decline and Mortality in Older People: A Community-Based Cohort Study. American journal of kidney diseases: the official journal of the National Kidney Foundation 2015 ;66(2):223-30.

20. Iff S, Wong G,Webster AC, Flood V, Wang JJ, Mitchell P et.al. Relative energy balance, CKD, and risk of cardiovascular and all-cause mortality. American journal of kidney diseases: the official journal of the National Kidney Foundation 2014;63(3):437-45.

**Table 1.** Patients Characteristics

|  |  |  |
| --- | --- | --- |
| Variable | GFR/Stage |  |
| G1 | G2 | G3a | G3b | G4 | G5 |  |
| Mean±SD | Mean±SD | Mean±SD | Mean±SD | Mean±SD | Mean±SD | p |
| Age,years | Gender | male | 81,7±5,8 | 80,6±3,9 | 81,7±5,8 | 80,6±3,9 | 82,6±5,0 | 82,5±4,7 | 0.106 |
| Female | 79,9±3,5 | 80,1±3,9 | 79,9±3,5 | 80,1±3,9 | 81,8±4,8 | 81,8±3,9 |
| Serum Ürea Nitrogen(mg/dL) | 19±8 | 21(±7) | 28(±13) | 39(±20) | 63(±28) | 87(±25) | 0.01 |
| Creatinine(mg/dL) | 0,64±0,1 | 0,87±0,1 | 1,18±0,17 | 1,56±0,2 | 2,42±0,55 | 4,88±2,09 | 0.01 |
| GFR(mL/kg/ 1.73 m2) | 109,1±18 | 72,4±8,1 | 52,2±4,2 | 37,8±4,6 | 23,1±4,4 | 11,1±3,2 | 0.01 |
| Hemoglobine(g/dL) | 11±3 | 11±3 | 11±3 | 11±2 | 11±2 | 11±2 | 0.01 |
| Hemotocrite(g/ dL) | 33±9 | 35±8 | 34±9 | 33±7 | 34±8 | 34±7 | 0.01 |
| No Comorbidity,n (%) | 111±2424(16,3%) | 73,7±964(43,5%) | 52,5±4,629(19,7%) | 38,8±4,121(14,3%) | 23,4±3,37(4,8%) | 12,5±2,12(1,4%) | 0.010 |
| MDS,n (%) | 136±364(16%) | 69±6,712(48%) | 48,1±3,43(12%) | 35,4±4,14(16%) | 20,7±6,12(8%) | 0 | 0.396 |
| Diabetes,n (%) | 105±11,521(12,7%) | 72,6±7,743(25,9%) | 51,8±3,627(16,3%) | 37,5±4,642(25,3%) | 23,2±4,418(10,8%) | 11±3,415(9%) | 0.020 |
| Alzheimer’s,n (%) | 112±1211(25%) | 74,6±7,89(20,5%) | 50,5±3,36(13,6%) | 35,7±56(13,6%) | 24,9±3,89(20,5%) | 8,1±43(6,8%) | 0.078 |
| CAD,n (%) | 103±0,62(9,5%) | 70,5±10,552,2±8(31%) | 52,2±5,52(9,5%) | 35,3±33(14,3%) | 24,5±6,73(14,3%) | 11,5±1,33(14,3%) | 0.690 |
| CVO,n (%) | 95,8±6,42(20%) | 69,61(10%) | 0 | 36,6±8,92(20%) | 16,91(10%) | 12±2,84(40%) | 0.046 |
| Arterial Hypertension,n (%) | 107±1527(16%) | 71±7,457(33,9%) | 52,6±4,524(14,3%) | 39,1±4,524(14,3%) | 22,2±4,519(11,3%) | 11,3±3,517(10,1%) | 0.341 |
| COPD,n (%) | 111,61(12,5%) | 74,9±172(25%) | 54±2,43(37,5%) | 0 | 21,9±5,22(25%) | 0 | 0.279 |
| Cancer,n (%) | 0 | 81,41(9,1%) | 56,9±2,12(18,2%) | 37,2±5,36(54,5%) | 28,51(9,1%) | 10,21(9,1%) | 0.034 |

MDS:Myelodysplastic syndrome, CAD: Coronary Artery Disease,CVO:Cerbrovasculer Disease, COPD: Chronic Obstrüctif Lung Diseas.

**Table 2.** Causes of Hospitalization by GFR Stage

|  |  |
| --- | --- |
| Reason For Hospıtalızatıon | GFR/STAGE |
| G1Mean±SD% | G2Mean±SD% | G3aMean±SD% | G3bMean±SD% | G4Mean±SD% | G5Mean±SD% | p٭ |
| Anemia | 110,9±18,635,9% | 71,4±7,933,0% | 51,5±4,240,6% | 37,6±4,534,3% | 22,9±5,521,0% | 10,9±2,911,1% | 0.030 |
| Hyperglisemia | 100,6±8,17,6% | 73±6,813,7% | 52,2±3,821,9% | 38±518,5% | 24,9±4,614,5% | 0 | 0.331 |
| Pnömonia | 104,4±8,34,3% | 78,1±7,74,6% | 55,5±3,82,1% | 40,2±1,52,8% | 271,6% | 0 | 0.541 |
| Üriner Enfection | 108,1±29,44,3% | 73,5±8,511,7% | 53,2±5,67,3% | 37,9±5,28,3% | 24,6±3,74,8% | 12,52,2% | 0.130 |
| Hyponatremia | 104,4±10,79,8% | 73,7±9,73,0% | 52,8±4,66,3% | 38,8±3,95,6% | 25,3±0,96,5% | 13,62,2% | 0.233 |
| Malnutrition | 109,5±22,227,2% | 72,3±8,621,8% | 53,4±311,3% | 38,7±4,220,3% | 25,7±2,413,5% | 0 | 0.000 |
| Acute Renal Failure | 1211,1% | 0 | 0 | 35,4±5,48,3% | 20,1±3,432,3% | 10,9±3,577,8% | 0.000 |
| Hypernatremia | 105,31,1% | 0 | 0 | 0 | 271,6% | 11,7±0,14,4% | 0.019 |
| Hypoglisemia | 1101,1% | 74,3±113,0% | 48,5±3,92,1% | 340,9% | 25,4±3,33,2% | 0 | 0.620 |
| Polycythemia | 91,41,1% | 69±3,12,5% | 53,4±7,92,1% | 0 | 0 | 0 | 0.354 |
| Gastroenteritis | 140,9±5,92,2% | 710,5% | 53,1±6,13,1% | 35,5±3,51,9% | 4,5±123,2% | 122,2% | 0.611 |

٭Fisher’s Exact test ,Pearson Chi-Square test

**Table 3.** Reason For Hospıtalızatıon and Comorbidite Factors Relationship

|  |  |
| --- | --- |
| Reason For Hospıtalızatıon | Comorbidities |
| Nonen | MDSn | Diabetesn | Alzheimer’sn | CADn | CVOn | Arterial Hypertensionn | COADn | Cancern | ٭p |
|  | Anemia % | 6935,8% | 2412,4% | 2412,4% | 147,3% | 73,6% | 21,0% | 4422,8% | 42,1% | 52,6% | 0.01 |
|  | hyperglisemia% | 22,4% | 11,2% | 7892,9% | 0 | 0 | 0 | 33,6% | 0 | 0 | 0.506 |
|  | pnömonia% | 631,6% | 0 | 736,8% | 0 | 0 | 0 | 526,3% | 15,3% | 0 | 0.545 |
|  | Üriner Enfection % | 1838,3% | 0 | 48,5% | 510,6% | 48,5% | 36,4% | 1327,7% | 0 | 0 | 0.02 |
|  | Hyponatremia % | 39,4% | 0 | 412,5% | 39,4% | 26,3% | 0 | 1753,1% | 13,1% | 26,3% | 0.07 |
|  | Malnutrition % | 3729,6% | 0 | 1512,0% | 1814,4% | 54,0% | 0 | 4636,8% | 21,6% | 21,6% | 0.01 |
|  | Acute Renal Failure % | 57,7% | 0 | 2132,3% | 34,6% | 34,6% | 46,2% | 2741,5% | 0 | 23,1% | 0.01 |
|  | hypernatremia% | 125,0% | 0 | 0 | 125,0% | 0 | 125,0% | 125,0% | 0 | 0 | 0.037 |
|  | hypoglisemia% | 18,3% | 0 | 1083,3% | 0 | 0 | 0 | 18,3% | 0 | 0 | 0.14 |
|  | Polycythemia % | 0 | 0 | 0 | 0 | 0 | 0 | 8100,0% | 0 | 0 | 0.08 |
|  | gastroenteritis% | 545,5% | 0 | 327,3% | 0 | 0 | 0 | 327,3% | 0 | 0 | 0.835 |

٭Pearson chi sq