RESEARCH PAPER

Differences in Urinary Neutrophil Gelatinase-Associated Lipocalin and Estimated Glomerular Filtration Rate in Patients with Chronic Kidney Disease

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ABSTRACT

Chronic Kidney Disease (CKD) engenders substantial morbidity due to deteriorating renal function. Estimated Glomerular Filtration Rate (eGFR) is the sine qua non for appraising nephric sufficiency, whilst NGAL has burgeoned as a more perspicacious biomarker for antecedent renal insult. This study aims to elucidate divergences in urinary NGAL concentrations and eGFR indices across disparate CKD nosological gradations. This observational cross-sectional inquiry encompassed 34 CKD-afflicted subjects at Airlangga University Hospital, Surabaya, June-July 2025. NGAL was quantified via enzyme-linked immunosorbent assay, and eGFR extrapolated pursuant to the CKD-EPI formula. ANOVA assessed differences between stages. The results showed that the subjects were predominantly 58 years old, with 22 male patients. The most common comorbidity was hypertension, with 10 patients (29.41%). The examination showed that the mean urinary NGAL level was 137.53 ng/mL, while the mean eGFR value was 34.55 mL/min/1.73 m². Analysis of Variance (ANOVA) test showed no significant difference in NGAL levels between CKD stages (p-value = 0.316), indicating that increasing stages were not followed by significant changes in NGAL. The results of the correlation analysis also showed that urinary NGAL was not related to eGFR Rate values (p-value > 0.05), the increase in NGAL seen in some stages was not in line with the degree of decline in kidney function indicated by eGFR. No significant difference was found between urine NGAL and eGFR. NGAL remains a potential biomarker for detecting and monitoring kidney damage with the eGFR

Keywords: CKD, NGAL, eGFR

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INTRODUCTION

Chronic kidney disease (CKD) is a condition typified by an insidious, protracted deterioration of renal function, hallmarked by a progressive and irreversible decrement in the glomerular filtration rate (GFR).[1] This nephric deterioration precipitates the body's incapacity to sustain metabolic homeostasis and fluid-electrolyte equilibrium, culminating in uraemic symptomatology.[2] This condition highlights the importance of early detection of decreased kidney function to prevent complications and slow disease progression.[3,4]

The estimated glomerular filtration rate (eGFR) is the primary method for assessing the severity of CKD, estimating the amount of blood filtered by the kidneys per minute.[5] This test has the advantage of detecting decreased kidney function early, even before changes in serum creatinine levels occur.[6] However, eGFR results are influenced by age, gender, race, and body mass index, often requiring repeated measurements to ensure accuracy.[7] Furthermore, a significant decline in eGFR typically only becomes apparent after kidney damage reaches approximately 50%, indicating the limitations of eGFR in detecting early kidney damage.[8] Neutrophil Gelatinase-Associated Lipocalin (NGAL) is a 25 kDa protein excreted in low amounts by various body tissues, including the kidneys. In kidney injury, NGAL levels increase more rapidly than serum creatinine, making it a potentially sensitive biomarker for renal tubular damage.[9] Although NGAL shows promise as an early indicator, the relationship between urinary NGAL levels and eGFR values across various stages of CKD has not been consistently defined.

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Therefore, this study aimed to analyze differences in urinary NGAL levels and eGFR values in CKD patients at various stages.[10]

METHOD

This constitutes an observational analytical inquiry employing a cross-sectional design, conducted spanning June through July 2025. Sampling and ascertainment of patient medical dossiers were undertaken at the Internal Medicine Clinic of Airlangga University Hospital, whilst Neutrophil Gelatinase-Associated Lipocalin (NGAL) and Estimated Glomerular Filtration Rate (eGFR) assays were operationalized at the Airlangga University Research Laboratory.

Urine samples were collected from chronic kidney disease patients registered at Airlangga University Hospital. eGFR was extrapolated via the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula predicated upon serum creatinine concentrations.[11] Urine NGAL examination was performed using the Enzyme-Linked Immunosorbent Assay (ELISA) method, with results expressed in ng/mL.[9] All procedures were carried out in accordance with clinical laboratory standards to ensure the reliability of the test results.

Research data were interrogated via Analysis of Variance (ANOVA) to appraise divergences in NGAL and eGFR concentrations across disparate CKD gradations, with a significance threshold of $p < 0.05$. Statistical scrutiny was operationalized utilizing the SPSS suite. This inquiry has procured ethical approbation from the Health Research Ethics Committee of the Faculty of Medicine, Airlangga University, bearing ethical certificate number 731/B/UN3.FK/I/PK.01/2025.

RESULTS

The chronic kidney disease (CKD) patients participating in this study had a mean age of 58.44 ± 12.0 years. Other data characteristics, such as the number of subjects in each age category, gender, and comorbidities in the subjects, are in Table 1.

Table 1. Characteristics of Study Subjects (n=34)

Characteristics	n(%)	(mean ± 2 SD)
Age		58,44±12,0 years
36-45	7(20,59%)	
46-55	6(17,65%)	
56-65	10(29,41%)	
>65	11(32,34%)	
Gender		
Male	22(64,7%)	
Female	12(35%)	
Type of comorbidity		
Hypertension	10(29,41%)	
Diabetes mellitus	3(8,8%)	
Heart	2(5,88)	
Hypertension and diabetes mellitus	12(35,29%)	
Hypertension and Heart	1(2,94%)	
Hypertension, diabetes, heart	3(8,8%)	

Based on Table 1, the characteristics of the study subjects show that the highest age was 58 years. The majority of subjects were male, amounting to 22 people.[12] The most common comorbidity found in this population was hypertension, which was recorded in 10 subjects. This finding indicates that the elderly group, especially men with a history of hypertension.[13]

Table 2. Analysis of eGFR Levels in CKD Patients

Stage CKD	n(%)	eGFR mL/min/1.73 m²) ± SD
Stage 1 and 2	7(20,6%)	75±12,63
Stage 3	11(32,4%0	42±81,82
Stage 4	5(14,7%)	19±98,34
Stage 5	11(32,4%)	9±23,00
Total	34	

The decline in eGFR in patients with chronic kidney disease (CKD) occurs due to progressive nephron loss and decreased glomerular filtration capacity. Each damaged nephron places an increased burden on the remaining nephrons, which, over time, undergo glomerular hypertrophy and sclerosis.[13] This accumulated damage leads to a decrease in the overall glomerular filtration rate, resulting in a decline in eGFR values from early to advanced stages.[14]

Table 3. NGAL Levels in CKD Patients

Stage CKD (ng/mL±SD)	Median	(min-max)	Mean
140,16±41,85			
130,73±23,12	135,085	93,636-200,34	137,54
131,72±26,57			
131,73±22,86			
Total	34		

Table 4 shows that PGK sufferers have NGAL levels of 93.636 ng/mL and a maximum of 200.340 ng/mL; the average value (mean) obtained is 137.54 ng/mL, which shows that the data is normally distributed.

Table 4. NGAL Levels at Various Stages

Stage CKD	EGFR (mL/min/1,73 m²)	NGAL (ng/mL) ±SD	P Value(significant)
Stage1 and 2	75±12,63	140,16±41,85	
Stage 3	42±82,81	130,73±23,12	
Stage 4	19±98,34	131,72±26,57	0,316
Stage 5	9±23,00	131,35±22,86	
Total	34		

The results showed that NGAL levels at various stages of CKD did not differ statistically. The decline in eGFR is usually slow, so in the early to middle stages, changes in values tend to be small between individuals. In contrast, urinary NGAL is a biomarker of renal tubular damage, which can increase more rapidly when the tubules are injured, but it also fluctuates due to transient factors such as renal blood flow, hydration, proteinuria, or glucose control. Because urinary NGAL is more sensitive to short-term tubular damage and eGFR reflects long-term filtration function, the two biomarkers do not always move in parallel at each stage of CKD.[15] In the same population, individual variations in tubular response or glomerular compensation can lead to relatively small differences in values between stages, resulting in statistically insignificant differences.[16]

Physiologically, NGAL is secreted by renal tubular epithelial cells in response to injury or oxidative stress. Increases in NGAL levels can occur rapidly, even before the appearance of glomerular filtration impairment. In contrast, eGFR represents the overall glomerular filtration capacity and tends to decline slowly with progressive nephron damage. This difference is what Changes in NGAL levels do not always align with changes in eGFR, especially in the early and intermediate stages of CKD.[17]

In the early stages of the disease, kidney damage is usually mild and partially reversible. The renal tubules may exhibit subclinical injury that triggers an increase in NGAL, while glomerular filtration function is still intact, so eGFR is not significantly reduced. In advanced stages, glomerular damage becomes predominant, while functional nephron mass has been significantly lost. At this stage, NGAL secretion may decrease due to a reduction in the number of active tubular cells, so NGAL levels do not always increase with disease progression.[18]

Individual differences in the etiology of CKD, such as those due to diabetes mellitus, hypertension, or obstructive nephropathy, can also influence NGAL levels. Each of these causes produces distinct patterns of injury between the glomeruli and tubules, contributing to variations in NGAL levels within each stage.[19] Clinically, there is a trend toward changes in NGAL levels, but statistically, differences between stages become insignificant due to the wide range of variation between individuals.[20]

CKD stages are determined by a wide range of eGFR, resulting in significant variation between individuals within a single stage. This variation also reduces the likelihood of statistically significant differences. Although NGAL and eGFR reflect different aspects of tubular and glomerular kidney damage, both biomarkers show similar trends across stages, particularly in the early and middle stages, so statistical differences are not apparen.[21]

The results of this study are in line with the research of Wasit et al, the study showed that NGAL levels increase along with the decline in kidney function, but

the differences between stages are not always statistically significant, this condition occurs because each patient has different causes and levels of kidney damage are not the same, in addition NGAL is more sensitive to short-term renal tubular injury, while eGFR shows the overall kidney filtering function which changes slowly in the long term.[22]

DISCUSSION

The decline in eGFR in patients with chronic kidney disease (CKD) occurs due to progressive nephron loss and decreased glomerular filtration capacity. Each damaged nephron increases the filtration load on the remaining nephrons, leading to glomerular hypertrophy and sclerosis. This accumulated damage causes a decline in overall kidney filtration function.[14] The results of this study show that eGFR values gradually decline from stage 1 to stage 5, consistent with the progressive and irreversible pathological mechanism of CKD.[23]

In the early stages of CKD, Neutrophil Gelatinase-Associated Lipocalin (NGAL) levels tend to increase. NGAL is a sensitive biomarker of renal tubular injury and increases earlier than eGFR decline.[18] However, in intermediate stages 3, NGAL levels may decrease due to a reduction in the number of healthy tubular cells capable of producing NGAL, as well as cellular adaptation to long-term stress.[24]

Meanwhile, in advanced stages (4 and 5), NGAL levels decline again. This decrease is thought to be due to a reduced number of functioning tubular cells and a decreased ability of the kidneys to respond to stress or injury.[25] The results of this study showed no significant difference in NGAL levels between stages of CKD.[26] This condition can be explained by the nature of NGAL, which better reflects acute tubular damage and fluctuates with transient factors such as hydration, renal blood flow, proteinuria, and glucose control, while eGFR reflects chronic and stable glomerular filtration function.[17] Because they reflect different aspects of kidney function, NGAL for short-term damage and eGFR for long-term damage, changes in both do not always align across stages of CKD.[24]

The study results showed that urinary NGAL levels did not differ at different eGFR levels because NGAL and eGFR reflect two different types of kidney damage. NGAL is more sensitive to sudden tubular damage, while eGFR indicates a slow, chronic decline in kidney function. Therefore, changes in NGAL do not align with the decline in eGFR. Furthermore, it is influenced by comorbidities in patients, such as hypertension or diabetes, which can cause the degree of tubular damage to vary even at similar CKD stages. In advanced stages, fewer remaining tubular cells also contribute to decreased NGAL production. NGAL values are also susceptible to changes due to other factors such as hydration, infection, protein in the urine, or changes in renal blood flow. These factors can obscure differences between patients' NGAL levels across CKD stages. The limited sample size of the study may also prevent small differences from being statistically significant.[22]

A limitation of this study is that urinary NGAL was not normalized against urinary creatinine. The NGAL ratio is important because urinary NGAL excretion is unstable and can fluctuate depending on urine volume. Without adjustment for urinary creatinine, NGAL values can be biased and do not reflect the true condition of the renal tubules. This instability in excretion may mask differences between stages of CKD that would be seen if the ratio to urinary creatinine were used. The results of this study show that eGFR values consistently decrease with increasing stages of chronic kidney disease, while urinary NGAL levels do not differ significantly between stages. This intimates that eGFR remains the preponderant parameter for appraising renal filtration sufficiency, whilst NGAL assumes a more pivotal role as a biomarker for the antecedent detection of tubular parenchymal insult. Subsequent inquiry employing a longitudinal design with an augmented sample cohort is advocated to fortify the validity of the nexus between NGAL and eGFR across disparate CKD gradations.

CONCLUSION

No significant difference was found between urine NGAL and eGFR. NGAL remains a potential biomarker for detecting and monitoring kidney damage with the eGFR.

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