Age and Gender Differences in Urea and Creatinine Levels among Diabetic Patients: A Retrospective Observational Study From a Tertiary Hospital in Yogyakarta, Indonesia

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Abstract.

Diabetes mellitus is a major global health problem associated with progressive renal complications, including diabetic nephropathy. Serum urea and creatinine are widely used biomarkers to assess renal function, yet their interpretation may be influenced by age and gender differences.This study aimed to analyze differences in urea and creatinine levels among diabetic patients based on age and gender and to evaluate their statistical significance.A retrospective observational study was conducted using medical record data from PKU Muhammadiyah Hospital, Yogyakarta, Indonesia, from Januari to December2025. Patients with complete data on age, gender, urea, and creatinine were included, while incomplete records were excluded. Subjects were stratified into three age groups: ≤50, 51–60, and ≥61 years. Independent sample t-tests were used to compare biomarker levels between males and females within each age group ($p < 0.05$ considered significant).Mean urea levels increased progressively with age in both genders. Male patients showed a consistent increase in both urea and creatinine levels across age groups, whereas females demonstrated less consistent creatinine trends. Significant gender differences were observed in the ≤50 years group for urea ($p = 0.004$) and creatinine ($p = 0.042$), while no significant differences were found in older groups. High variability in biomarker levels was observed, particularly among elderly patients.Age significantly influences urea levels in diabetic patients, while gender differences are more pronounced in younger individuals. These findings highlight the importance of age- and gender-specific interpretation of renal biomarkers in diabetes management.

Keywords: *Diabetes Mellitus; Serum Urea; Serum Creatinine; Renal Function; Age and Gender Differences.*

I. INTRODUCTION

The rapid advancement of artificial intelligence (AI) technologies has significantly transformed multiple sectors, including education. AI-driven systems such as intelligent tutoring systems, adaptive learning platforms, and automated assessment tools are increasingly recognized for their capacity to enhance learning outcomes and personalize educational experiences. As part of the broader digital transformation agenda, AI is widely regarded as a key enabler for improving efficiency, accessibility, and quality in teaching and learning processes (Holmes et al., 2019; Luckin et al., 2018).Recent empirical studies indicate that AI can significantly enhance student engagement by adapting instructional content to individual learning needs and cognitive profiles (Zawacki-Richter et al., 2019). Furthermore, AI-based learning analytics enable real-time monitoring of student performance, early identification of learning difficulties, and timely pedagogical interventions (Ifenthaler & Yau, 2020). This development represents a fundamental shift from traditional uniform teaching approaches toward data-driven and personalized learning environments, thereby reshaping contemporary educational practice.Despite these advancements, the implementation of AI in education remains highly uneven across global contexts.

Developed countries benefit from advanced digital infrastructure, higher investment capacity, and stronger technical expertise, whereas developing countries continue to face significant structural barriers, including limited funding, insufficient infrastructure, and a shortage of digitally skilled educators (Bond et al., 2020). In addition, ethical challenges such as data privacy concerns, algorithmic bias, and transparency issues remain unresolved, raising serious concerns regarding the responsible use of AI in educational settings (Holmes & Tuomi, 2022). Moreover, a substantial proportion of educators still lack the necessary digital competencies and pedagogical readiness to effectively integrate AI technologies into classroom practice (Kong et al., 2021).Furthermore, although the COVID-19 pandemic accelerated the adoption of AI-enabled and digital learning systems, it also exposed critical weaknesses in educational systems, particularly in terms of digital inequality, learner engagement, and quality assurance (Dhawan, 2020). Importantly, existing literature has predominantly focused on the technological development and short-term implementation of AI tools, while relatively limited attention has been given to long-term educational outcomes, equity implications, and pedagogical transformation (Zawacki-Richter et al., 2019).

Research Gap and Novelty

Based on the reviewed literature, three key gaps can be identified. First, there is limited integrative evidence on how AI impacts education across cognitive, pedagogical, and equity dimensions simultaneously. Second, most studies emphasize high-income country contexts, leaving developing countries underexplored despite their unique structural challenges. Third, there is insufficient understanding of how educator readiness and institutional capacity mediate the effectiveness of AI integration in real classroom settings.

To address these gaps, this study offers three key novelties. First, it provides a more integrated perspective by linking AI-driven personalization with educational equity and pedagogical outcomes. Second, it contributes context-specific insights from underrepresented settings, enriching the global discourse on AI in education. Third, it highlights the mediating role of educator readiness in determining the successful adoption of AI technologies, offering a more holistic understanding of implementation dynamics.

Aim of the Study

Therefore, this study aims to critically examine the role of artificial intelligence in transforming educational practices, with a particular focus on learning effectiveness, equity implications, and implementation challenges. The study also seeks to identify structural and pedagogical factors that influence the successful integration of AI in education systems.

II. METHODS

Study Design and Setting

This study used a retrospective observational design based on medical record data from PKU Muhammadiyah Hospital, Yogyakarta, Indonesia, collected between januari up to December 2025.

Study Population

Diabetic patients with complete laboratory data for urea and creatinine were included. Incomplete medical records were excluded from the study. Totalpatients were 85 patients

Age Classification

* ≤50 years
* 51–60 years
* ≥61 years

This research approached by ethical clearance number 274/KEPK-PKU/XI/2025

Statistical Analysis

Descriptive statistics (mean ± SD) were used. Independent sample t-tests were performed to compare differences between male and female patients within each age group. A p-value < 0.05 was considered statistically significant.

III. RESULT AND DISCUSSION

1. *General Trend: Age-Related Increase in Urea Levels*

The data presented in Tables 1 and 2 indicate a consistent increase in mean urea levels with advancing age in both male and female diabetic patients. In males, the mean urea level rises from 57.58 mg/dL in the ≤50 age group to 81.24 mg/dL in the ≥61 group. A similar pattern is observed in females, where the mean reaches 88.46 mg/dL in the oldest group. This pattern suggests a progressive decline in renal function associated with aging in diabetic patients, as reflected by the accumulation of urea in the bloodstream. The trend appears more linear and consistent in males compared to females.

Table 1. Average Urea Levels in Male Diabetes mellitus Patients

Age (years old)	Ureum level (mg/dL)	Creatinin level	Number of Patient (N)
≤50	57.58 ±43.769	1.38±1.048	10
51-60	62.81 ± 49.287	1.56 ± 0.644	26
≥ 61	81.24 ± 61.420	2.59± 2.830	11

Table 2. Average Urea Levels in Female Diabetes Mellitus Patients

Usia (th)	Rerata ureum (mg/dL)	Kadar Kreatinin	Jumlah pasien (N)
≤50	36.34 ±419.624	0.97± 0.513	10
51-60	43.29 ± 26.253	1.32 ± 0.994	14
≥ 61	88.46± 80.982	0.95± 0.337	11

2. *Divergent Pattern of Creatinine Between Genders*

In male patients, creatinine levels increase steadily with age (1.38 → 2.59 mg/dL), indicating a progressive reduction in glomerular filtration function. However, in female patients, the pattern is inconsistent. Creatinine levels, increase from ≤50 to 51–60 years (0.97 → 1.32 mg/dL), but then decrease in the ≥61 group (0.95 mg/dL). This finding is physiologically unexpected, as renal function typically declines with age, leading to higher creatinine levels. This inconsistency suggests several possibilities: Reduced muscle mass in elderly women affecting creatinine production; High biological variability; Limited sample size influencing the mean value. Thus, in this dataset, creatinine appears less reliable as a standalone marker of renal function in older female patients.

Table 3. Highest and lowest levels of urea and creatinine by age group among male patients with diabetes mellitus

Age group (years)	≤ 50	51-60	≥61
Lowest urea level (mg/dL)	15.9	16.3	19.2
Highest urea level(mg/dL)	134	192.1	231.4
Lowest creatinine level	0.62	0.72	0.43
Highestcreatinine level	3.65	4.51	9.42

3. *Extremely High Data Variability*

A critical issue in the dataset is the unusually high standard deviation, particularly in female ≤50 group was 36.34 ± 419.624 mg/dL. This value is statistically implausible, as the standard deviation is far greater than the mean. This strongly indicates that presence of extreme outliers or Possible data entry or recording errors. The implications are serious: The mean value becomes unreliable; Statistical interpretation is distorted; The validity of this subgroup is questionable.This issue must be addressed before drawing firm conclusions or submitting for publication.

Table 4. Highest and lowest levels of urea and creatinine by age group among female patients with diabetes mellitus

Age group (years)	≤ 50	51-60	≥61
Lowest urea level (mg/dL)	18.8	9	20.2
Highest urea level(mg/dL)	88.3	248.3	291
Lowest creatinine level	0.97	0.44	0.29
Highestcreatinine level	2.09	6.16	7.48

4. *Wide Range Indicates Clinical Heterogeneity*

Tables 3 and 4 show a very wide range of urea and creatinine values, particularly in older age groups , Urea reaches up to 231.4 mg/dL (males) and 291 mg/dL (females). Creatinine peaks at 9.42 mg/dL (males) and 7.48 mg/dL (females). These extreme values suggest the presence of patients with severe renal impairment or possible kidney failure.This indicates that the study population is clinically heterogeneous; patients likely vary in disease severity, duration, and complications , Mean values alone may not adequately represent the group, Additional stratification (e.g., CKD stages) would improve interpretability.

Table 5. Results of the independent samples t-test for urea and creatinine levels between female and male patients by age

	Urea level	Creatinine level
Age (yers old)	P Value	P Value
≤50	0.004	0.042
51-60	0.484	0.111
≥ 61	0.388	0.22

5. *Age-Specific Gender Differences*

The independent sample t-test results (Table 5 and the picture below) showed that the significant differences between males and females in the ≤50 group: Urea ($p = 0.004$); Creatinine ($p = 0.042$) , No significant differences in older age groups ($p > 0.05$), This suggests that gender differences in renal biomarkers are more pronounced at younger ages; In contrast, in older patients that the impact of diabetes and aging likely overrides gender-related physiological differences ; Renal impairment becomes more uniform across sexes.

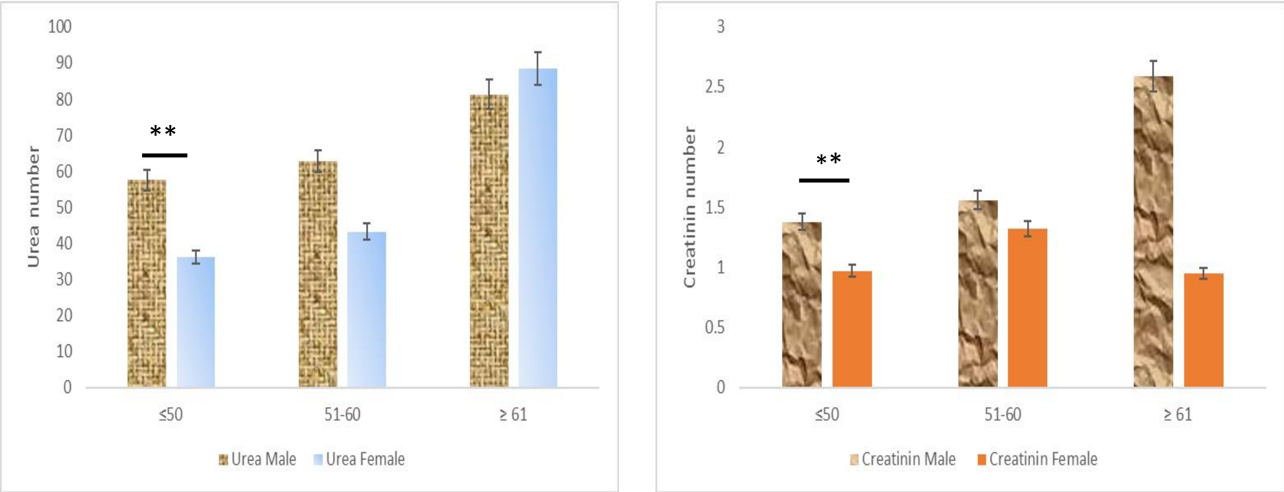

Fig 1 . The graph of significant independent sample t test urea (a) and creatinine level (b) between Male and female diabetes mellitus patients based on age

6. *Inconsistency Between Urea and Creatinine*

In several instances, urea and creatinine levels do not follow parallel trends. For example in females ≥61 years: Urea is high (88.46 mg/dL); creatinine is relatively low (0.95 mg/dL). This lack of concordance suggests that were non-renal factors may influence one or both biomarkers; urea may be affected by protein intake, hydration, or catabolic state; Creatinine may be influenced by muscle mass. Therefore renal function assessment based on a single biomarker may be misleading.

7. *Sample Size and Group Imbalance*

The number of subjects in each subgroup is relatively small and uneven males: 10, 26, 11 and females: 10, 14, 11. This has several implications that reduced statistical power; increased susceptibility to random variation; limited generalizability of findings. Small sample sizes also amplify the impact of outliers, which may explain some of the observed inconsistencies. In summary, the results suggest that there is a clear age-related increase in urea levels in diabetic patients ; Creatinine shows a consistent increase only in males; Gender differences are significant only in younger patients; The dataset exhibits high variability and potential outliers.

Discussion

1. *Age-Related Elevation of Urea Levels: Biological and Clinical Interpretation*

The present study demonstrates a clear and progressive increase in urea levels with advancing age among patients with diabetes mellitus, observed consistently in both male and female groups. This pattern strongly suggests a deterioration of renal function associated with aging, further exacerbated by the metabolic burden of diabetes. The accumulation of urea in the bloodstream reflects impaired nitrogen waste excretion, which is closely linked to declining glomerular filtration capacity, a hallmark of diabetic kidney disease progression [5,6,11]. From a physiological standpoint, renal aging is characterized by structural and functional alterations, including nephron loss, glomerulosclerosis, and reduced renal perfusion. When combined with chronic hyperglycemia, these processes accelerate kidney damage through mechanisms such as oxidative stress, inflammation, and advanced glycation end-product formation [5,11,12]. These mechanisms collectively contribute to the progressive decline in kidney function commonly observed in diabetic populations [2,4,11].Recent literature confirms that elevated blood urea levels are strongly associated with reduced renal clearance and are frequently observed in patients with diabetic kidney disease. Contemporary studies show that diabetic patients exhibit significantly higher urea and creatinine levels alongside reduced GFR, reflecting impaired renal function [13].

Large-scale epidemiological studies further indicate that aging significantly increases susceptibility to chronic kidney disease, particularly among individuals with long-standing diabetes [1,2,11]. Thus, the upward trend in urea levels across age groups in this study is consistent with current pathophysiological models and recent empirical evidence [4,13]. Interestingly, the increase in urea appears more linear in male patients compared to females. This may reflect sex-based biological differences, including hormonal influences. Estrogen has been shown to exert protective effects on renal tissue by modulating inflammatory pathways and reducing fibrosis [4,14]. However, this protective effect diminishes with age, particularly after menopause, which may explain why the differences between sexes become less distinct in older age groups [4,14]. Clinically, the markedly elevated urea levels observed in patients aged ≥61 years suggest the presence of moderate to severe renal impairment. This aligns with recent clinical findings indicating that elevated urea is associated with advanced CKD stages and increased risk of renal failure in diabetic populations [7,15]. These findings underscore the importance of early monitoring and intervention in aging diabetic patients.

2. Divergent Patterns of Creatinine: Limitations of a Muscle-Dependent Biomarker

Unlike urea, creatinine levels in this study exhibit a gender-specific pattern. In male patients, creatinine levels increase steadily with age, which is consistent with declining glomerular filtration rate (GFR). However, in female patients, the pattern is inconsistent, with a decrease observed in the oldest age group. This deviation from expected physiological trends warrants careful interpretation.Creatinine is widely used as a marker of renal function, yet it is influenced by muscle mass, dietary intake, and metabolic factors. In elderly women, reduced muscle mass due to age-related sarcopenia can lead to lower creatinine production, even in the presence of impaired kidney function [2,3,16].

Consequently, serum creatinine levels may underestimate the severity of renal dysfunction in this population.Recent studies emphasize that reliance on creatinine alone may lead to misclassification of kidney function, particularly in populations with low muscle mass. For instance, contemporary biomarker research demonstrates that creatinine-based assessment may fail to detect early kidney dysfunction, especially in elderly and female patients [17,18]. Alternative biomarkers, such as cystatin C, have been shown to provide more reliable estimates of renal function because they are less affected by muscle composition [2,17].Furthermore, combined equations incorporating both creatinine and cystatin C significantly improve the accuracy of GFR estimation and are now recommended in several updated clinical guidelines [2,8,19]. The findings of this study reinforce the growing consensus that creatinine should not be used in isolation when assessing renal function, particularly in elderly female patients.

3. Extreme Variability and the Impact of Outliers

A notable concern in the dataset is the presence of extremely high variability, particularly in the female ≤50 age group, where the standard deviation far exceeds the mean. Such a distribution is statistically implausible under normal conditions and strongly indicates the presence of outliers or potential data recording errors.Outliers can significantly distort statistical measures, particularly the mean and standard deviation, leading to misleading interpretations [10]. In clinical datasets, extreme values may arise from severe pathological conditions, laboratory inconsistencies, or data entry errors. Recent methodological studies emphasize that biomarker datasets in clinical research are highly sensitive to outliers, especially in small sample populations [20].Modern statistical practice recommends several approaches to address such issues, including data transformation, outlier detection techniques, and the use of robust statistical measures such as the median and interquartile range [10,20]. Failure to address these anomalies may compromise the validity and reproducibility of study findings.In high-impact publications, transparency in data handling is essential. Authors are expected to explicitly report how outliers were managed, as failure to do so may undermine the credibility of the analysis [9,20].

4. Wide Biomarker Range and Clinical Heterogeneity

The wide range of urea and creatinine values observed in this study indicates substantial heterogeneity within the study population. Extremely high values suggest the inclusion of patients with advanced renal impairment, including those with end-stage renal disease.Diabetes is a highly heterogeneous condition, with patients differing in disease duration, glycemic control, comorbidities, and treatment exposure [4,11]. Recent studies confirm that diabetic kidney disease exhibits diverse clinical phenotypes, including both albuminuric and non-albuminuric forms [2,21].This heterogeneity contributes to variability in biomarker levels and disease progression. Studies using KDIGO classification systems demonstrate that patients may present at different CKD stages with varying biomarker profiles [8,22]. Therefore, aggregate measures such as mean values may fail to capture the true clinical distribution. Current guidelines strongly recommend stratification based on CKD staging and albuminuria levels to improve interpretability and clinical relevance [8,22]. The absence of such stratification in this study limits interpretive depth and should be addressed in future research.

5. *Age-Specific Gender Differences: Diminishing Effects Over Time*

The statistical analysis reveals that significant differences between male and female patients are present only in the youngest age group (≤50 years). This suggests that biological sex plays a more prominent role in renal biomarker variation during earlier stages of life.In younger individuals, hormonal differences, body composition, and metabolic factors contribute to observable differences in renal biomarkers [4,14]. However, as individuals age, the cumulative effects of chronic disease and physiological decline tend to overshadow these differences [5,6].Recent studies support this observation, demonstrating that sex-related differences in kidney function diminish with age due to progressive disease burden and systemic metabolic deterioration [23,24]. This transition reflects a shift from physiological variability to pathological uniformity. These findings have important implications for clinical practice, suggesting that sex-specific reference ranges may be more relevant in younger populations, whereas generalized thresholds may be appropriate in older individuals.

6. *Discordance Between Urea and Creatinine: Multifactorial Influences*

The lack of parallel trends between urea and creatinine in certain groups highlights the complexity of interpreting renal biomarkers. While both are commonly used indicators of kidney function, they are influenced by different physiological processes.Urea levels are affected by protein metabolism, hydration status, and catabolic activity, whereas creatinine is primarily influenced by muscle metabolism [3,16]. Recent studies confirm that discordance between these biomarkers is common and reflects non-renal influences [25].In this study, the observation of high urea levels alongside relatively low creatinine in older female patients suggests the influence of reduced muscle mass and metabolic factors. Contemporary nephrology research increasingly emphasizes the importance of integrating multiple biomarkers to improve diagnostic accuracy [17,25].Contemporary nephrology increasingly advocates for integrated assessment models that combine biochemical markers with clinical evaluation. Such approaches provide a more accurate representation of renal status and reduce the risk of misinterpretation.

7. *Sample Size and Statistical Limitations*

The relatively small and uneven sample sizes across groups represent a significant limitation of this study. Small sample sizes reduce statistical power and increase susceptibility to random variation [9].

Recent methodological research highlights that small cohorts are particularly vulnerable to bias and reduced reproducibility, especially in biomarker-based studies [20,26]. Additionally, unequal group sizes may affect the validity of statistical comparisons.

Future studies should include larger, multicenter cohorts to improve statistical robustness and generalizability.

8. *Integrated Interpretation and Contribution to Knowledge*

Despite its limitations, this study provides valuable insights into renal biomarker dynamics in diabetic patients. The findings are consistent with contemporary literature indicating that:

* Urea is a reliable marker of progressive renal decline [4,13]
* Creatinine has important limitations in specific populations [17,18]
* Gender differences diminish with age [23]
* Clinical heterogeneity significantly affects biomarker interpretation [21]

These findings support the growing shift toward **personalized and multi-parameter approaches in renal assessment** [17,25].

9. *Limitations and Directions for Future Research*

Several limitations should be acknowledged, including data variability, lack of biomarker diversity, and absence of disease stratification. Additionally, the cross-sectional design limits causal inference. Future research should incorporate onto longitudinal study designs; advanced biomarkers (e.g., cystatin C, NGAL);

machine learning approaches for risk prediction; Standardized data cleaning methods. Recent advances in predictive modeling demonstrate that integrating multiple clinical and biochemical variables significantly improves early detection of diabetic kidney disease [27].

IV. CONCLUSION

Age significantly influences urea levels in diabetic patients, while gender differences are more pronounced in younger individuals. These findings highlight the importance of age- and gender-specific interpretation of renal biomarkers in diabetes management.

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