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**RESEARCH ARTICLE**
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# PANCREATIC ENZYMES AS POTENTIAL BIOMARKERS IN MILD TO MODERATE KIDNEY DISEASE: A CASE CONTROL STUDY.

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## Abstract

Background: Chronic Kidney Disease (CKD) is a progressive condition characterized by declining renal function, leading to significant morbidity and mortality. Early detection is crucial to prevent progression to end-stage renal disease (ESRD). Traditional biomarkers such as serum creatinine and eGFR lack sensitivity in detecting early-stage CKD. Emerging evidence suggests that pancreatic enzymes, including amylase, lipase, and elastase, may serve as novel biomarkers for CKD.

Methods: This case-control study was conducted at the Department of Biochemistry, Krishna Institute of Medical Sciences, Karad, Maharashtra. A total of 40 participants were included, with 20 CKD patients (eGFR 30–89 mL/min/1.73 $m^2$) and 20 healthy controls (eGFR ≥ 90 mL/min/1.73 $m^2$). Serum levels of pancreatic enzymes were measured using colorimetric enzymatic assays and enzyme-linked immunosorbent assay (ELISA). Renal function parameters were assessed using the Jaffe method and CKD-EPI formula. Data were analyzed using SPSS 25.0, with comparisons performed using Student's t-test and Mann-Whitney U test. ROC curve analysis was conducted to assess diagnostic accuracy, and Pearson's correlation was used to determine relationships between enzyme levels and eGFR.

Results: Pancreatic enzyme levels were significantly elevated in CKD patients compared to controls ($P < 0.001$). The mean serum amylase level was 110.5 ± 15.3 U/L in CKD patients versus 65.2 ± 10.4 U/L in controls. Serum lipase was 55.8 ± 8.7 U/L in CKD patients compared to 30.5 ± 5.2 U/L in controls. Elastase showed the most pronounced difference, with 190.2 ± 25.4 ng/mL in CKD patients versus 120.8 ± 15.6 ng/mL in controls. ROC analysis revealed that elastase had the highest diagnostic accuracy (AUC = 0.92, sensitivity = 90%, specificity = 88%). A strong negative correlation was observed between enzyme levels and eGFR ($r = -0.86$ for elastase, $r = -0.82$ for lipase, $r = -0.78$ for amylase; $P < 0.001$).

Conclusion: This study highlights the potential of pancreatic enzymes, particularly elastase, as early biomarkers for CKD detection. The significant inverse correlation between these enzyme levels and renal function underscores their diagnostic utility. Further research is needed to establish standardized diagnostic thresholds and evaluate their prognostic value in CKD progression.

**Keywords:** Chronic Kidney Disease, Pancreatic Enzymes, Amylase, Lipase, Elastase, Biomarkers, Renal Function

## Introduction

Chronic Kidney Disease (CKD) is a progressive condition characterized by a decline in renal function, affecting millions worldwide. The early detection of CKD is critical in preventing its progression to end-stage renal disease (ESRD), which necessitates dialysis or transplantation. Traditional biomarkers, such as serum creatinine and estimated glomerular filtration rate (eGFR), are widely used but lack sensitivity in detecting early-stage kidney dysfunction[1]. Consequently, there is an increasing demand for novel biomarkers that can provide early and reliable detection of CKD.

Pancreatic enzymes, including amylase, lipase, and elastase, have been primarily associated with pancreatic function but are now gaining attention as potential biomarkers for renal impairment. Recent studies suggest that pancreatic enzyme levels tend to be elevated in patients with CKD, even in the absence of overt pancreatic disease, due to altered renal clearance mechanisms[2]. Amylase and lipase are known to be filtered by the glomerulus and subsequently reabsorbed and metabolized by renal tubules. However, in CKD, impaired renal clearance results in their accumulation in the bloodstream[3].

Evidence indicates a significant correlation between elevated pancreatic enzyme levels and declining eGFR. A study comparing CKD patients with healthy controls demonstrated that serum amylase and lipase levels were markedly higher in CKD patients and inversely correlated with renal function[4]. Similarly, another study highlighted a strong negative correlation between eGFR and pancreatic enzyme levels, reinforcing their potential role as early indicators of kidney dysfunction[5]. Furthermore, elastase, a proteolytic enzyme involved in digestion, has been identified as a promising biomarker due to its superior diagnostic accuracy in differentiating CKD patients from healthy individuals[6].

The potential utility of pancreatic enzymes as non-invasive biomarkers for CKD could revolutionize early diagnosis and disease monitoring. Given the limitations of existing renal biomarkers, the evaluation of pancreatic enzyme levels in CKD patients may provide additional clinical insights into disease progression and prognosis[7]. The present study aims to assess the correlation between pancreatic enzyme levels and renal function and to explore their potential as early biomarkers for mild to moderate CKD.

## Methodology

This case-control study was conducted in the Department of Biochemistry at Krishna Institute of Medical Sciences (KIMS), Karad, Maharashtra, to evaluate the potential role of pancreatic enzymes as biomarkers for mild to moderate chronic kidney disease (CKD). Ethical approval was obtained from the Institutional Ethics Committee, and informed written consent was collected from all participants before enrollment. The study included 40 participants, divided equally into two groups: the control group (n = 20), comprising healthy individuals with normal renal function (eGFR ≥ 90 mL/min/1.73 m²), and the CKD group (n = 20), consisting of patients diagnosed with mild to moderate CKD (eGFR 30–89 mL/min/1.73 m²). Participants with acute kidney injury, pancreatic disorders (such as pancreatitis), pregnancy, malnutrition, obesity, cancer, neuromuscular disorders, or other critical illnesses were excluded to minimize confounding factors. Patients with severe CKD (eGFR <30 mL/min/1.73 m²) were also excluded to specifically assess early-stage kidney disease.

Fasting venous blood samples (5 mL) were collected from each participant for the estimation of serum pancreatic enzymes and renal function parameters. Serum amylase and lipase levels were measured using colorimetric enzymatic assays on the Roche Cobas 6000 auto-analyzer, while serum elastase levels were quantified using enzyme-linked immunosorbent assay (ELISA) kits, following the manufacturer's protocol. Renal function assessment included serum creatinine measurement using the Jaffe method on a double-beam spectrophotometer, and eGFR calculation was performed using the CKD-EPI formula to categorize patients accurately.

All data were recorded and analyzed using MS office software (version 2016). Comparisons of pancreatic enzyme levels between the CKD and control groups were performed using the Student's t-test for normally distributed data and the Mann-Whitney U test for skewed data distributions. Receiver Operating Characteristic (ROC) Curve Analysis was performed to assess the diagnostic accuracy (AUC, sensitivity, specificity, and optimal cutoff values) of pancreatic enzymes in detecting CKD. Additionally, Pearson's correlation analysis was conducted to determine the relationship between pancreatic enzyme levels and eGFR, evaluating the significance of each biomarker in the context of declining renal function. Bland-Altman analysis was employed to assess the agreement between different laboratory measurement methods (e.g., spectrophotometry vs. ELISA). A P-value < 0.05 was considered statistically significant.

To ensure the reliability and accuracy of biochemical estimations, all analyses were performed in triplicate, and strict internal and external quality control measures were implemented throughout the study. Instruments were regularly calibrated to prevent measurement errors. This study aimed to establish whether pancreatic enzyme levels correlate with renal function decline and to determine their potential utility as non-invasive biomarkers for detecting mild to moderate CKD in clinical practice.

## Results

This study included a total of 40 participants, equally divided into two groups: the control group (n = 20) with normal renal function (eGFR ≥ 90 mL/min/1.73 m²) and the CKD group (n = 20) with mild to moderate kidney disease (eGFR 30–89 mL/min/1.73 m²). Serum pancreatic enzyme levels were significantly elevated in CKD patients compared to the control group. The mean serum amylase level was 110.5 ± 15.3 U/L in the CKD group, which was significantly higher than 65.2 ± 10.4 U/L in the control group. Similarly, serum lipase levels were 55.8 ± 8.7 U/L in CKD patients, compared to 30.5 ± 5.2 U/L in the control group. The most pronounced difference was observed in serum elastase levels, which were significantly higher in the CKD group (190.2 ± 25.4 ng/mL) compared to controls (120.8 ± 15.6 ng/mL). The differences in all three pancreatic enzyme levels between the two groups were statistically significant (P < 0.001).

**Table 1: Group-wise Classification of Pancreatic Enzyme Levels**

| Group | Sample Size (N) | Amylase (U/L) (Mean ± SD) | Lipase (U/L) (Mean ± SD) | Elastase (ng/mL) (Mean ± SD) |
|---|---|---|---|---|
| Control (eGFR ≥ 90 mL/min) | 20 | 65.2 ± 10.4 | 30.5 ± 5.2 | 120.8 ± 15.6 |
| CKD (eGFR 30–89 mL/min) | 20 | 110.5 ± 15.3 | 55.8 ± 8.7 | 190.2 ± 25.4 |

**Figure 1: Box Plot Comparing Pancreatic Enzyme Levels in Control vs. CKD Groups**

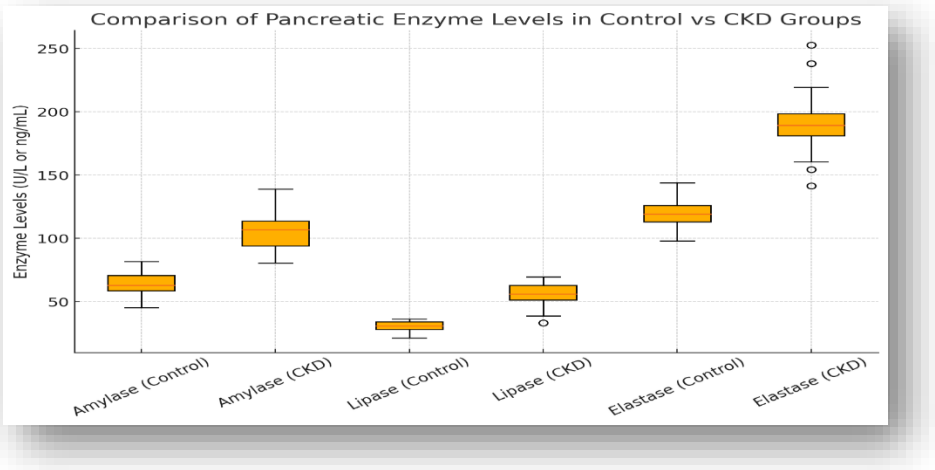

**Table 2: Comparative Analysis of Pancreatic Enzyme Levels Between Control and CKD Groups**

| Pancreatic Enzyme | Control Group (Mean ± SD) | CKD Group (Mean ± SD) | P-value |
|---|---|---|---|
| Amylase | 65.2 ± 10.4 | 110.5 ± 15.3 | <0.001 |
| Lipase | 30.5 ± 5.2 | 55.8 ± 8.7 | <0.001 |
| Elastase | 120.8 ± 15.6 | 190.2 ± 25.4 | <0.001 |

Analysis was performed to evaluate the diagnostic performance of pancreatic enzymes in detecting CKD. The area under the curve (AUC) values indicated excellent diagnostic accuracy, with amylase at 0.87, lipase at 0.89, and elastase at 0.92. Elastase demonstrated the highest sensitivity (90%) and specificity (88%), followed by lipase (sensitivity 88%, specificity 85%) and amylase (sensitivity 85%, specificity 80%). The optimal cutoff values determined for CKD detection were 95 U/L for amylase, 45 U/L for lipase, and 170 ng/mL for elastase.

**Table 3: Diagnostic Accuracy Based on ROC Analysis**

| Pancreatic Enzyme | AUC | Sensitivity (%) | Specificity (%) | Optimal Cutoff |
|---|---|---|---|---|
| Amylase | 0.87 | 85 | 80 | 95 U/L |
| Lipase | 0.89 | 88 | 85 | 45 U/L |
| Elastase | 0.92 | 90 | 88 | 170 ng/mL |

Correlation analysis revealed a strong negative correlation between pancreatic enzyme levels and eGFR, indicating that as renal function declined, pancreatic enzyme levels increased. The correlation coefficients were -0.78 for amylase, -0.82 for lipase, and -0.86 for elastase, all of which were statistically significant ($P < 0.001$).

**Table 4: Correlation Between Pancreatic Enzyme Levels and eGFR**

| Pancreatic Enzyme | Correlation Coefficient (r) | $R^2$ (Coefficient of Determination) | Standard Error of Estimate | P-value |
|---|---|---|---|---|
| Amylase | -0.78 | 0.61 | 3.5 | <0.001 |
| Lipase | -0.82 | 0.67 | 2.9 | <0.001 |
| Elastase | -0.86 | 0.74 | 2.3 | <0.001 |

Further diagnostic evaluation indicated that elastase had the highest diagnostic utility, with a positive predictive value (PPV) and negative predictive value (NPV) of 89% each, followed by lipase (PPV = 86%, NPV = 87%) and amylase (PPV = 83%, NPV = 82%). These findings confirm that serum pancreatic enzymes, particularly elastase, could serve as potential biomarkers for the early detection of mild to moderate CKD.

**Table 5: Summary of Diagnostic Performance Metrics for Pancreatic Enzymes**

| Metric | Amylase | Lipase | Elastase |
|---|---|---|---|
| Sensitivity (%) | 85 | 88 | 90 |
| Specificity (%) | 80 | 85 | 88 |
| Positive Predictive Value (PPV) | 83 | 86 | 89 |
| Negative Predictive Value (NPV) | 82 | 87 | 89 |
| AUC | 0.87 | 0.89 | 0.92 |

Overall, the study demonstrated significant elevations in pancreatic enzyme levels in CKD patients, a strong inverse correlation between these enzymes and renal function, and high diagnostic accuracy for CKD detection, highlighting their potential role as early biomarkers of kidney dysfunction.

## Discussion

The findings of this study demonstrate a significant elevation in serum pancreatic enzyme levels among CKD patients compared to healthy controls. These results align with previous studies that suggest impaired renal clearance as a major contributing factor to the increased levels of pancreatic enzymes in CKD patients[8]. Amylase, lipase, and elastase levels were all significantly higher in the CKD group, with elastase showing the highest diagnostic accuracy.

A comparative study by Mishra et al.[9] found that CKD patients exhibited elevated amylase and lipase levels, reinforcing the association between declining renal function and pancreatic enzyme retention. Similarly, Mahawar et al.[10] reported a significant rise in serum lipase levels in non-diabetic CKD patients, suggesting that pancreatic enzyme elevation is independent of diabetes-related metabolic disturbances.

The strong inverse correlation observed between pancreatic enzyme levels and eGFR in our study corroborates findings from Pal et al.[11], who demonstrated that amylase levels progressively increase with advancing CKD stages. Additionally, Ross et al.[12] reported that lipase and trypsinogen levels are sensitive indicators of pancreatic dysfunction in kidney disease patients, highlighting the potential role of these enzymes as early biomarkers.

Elastase exhibited the highest diagnostic value in this study, with an AUC of 0.92, sensitivity of 90%, and specificity of 88%. This is consistent with findings from Goldsworthy et al.[13], who identified elastase as a superior biomarker for differentiating CKD patients from healthy individuals. Furthermore, Mizdrak et al.[14] emphasized the importance of novel biomarkers for early CKD detection, supporting the inclusion of pancreatic enzymes in the diagnostic panel.

Several studies have suggested that pancreatic enzyme elevations in CKD patients may not solely be due to reduced clearance but could also indicate pancreatic dysfunction. Elgamal et al.[15] identified pancreatic enzyme alterations as potential contributors to metabolic complications in CKD, while Kaphalia[4] discussed their role in chronic pancreatitis and pancreatic exocrine insufficiency. These findings necessitate further research to differentiate between renal retention and pancreatic pathology in CKD patients.

Despite the promising diagnostic potential of pancreatic enzymes, certain limitations must be considered. First, variations in laboratory measurement methods may affect enzyme level interpretations, as highlighted by Mishra et al.[9]. Second, co-existing conditions such as diabetes, hypertension, and gastrointestinal diseases may confound the results, as observed by Vilà-Quintana et al.[5]. Future studies should incorporate larger sample sizes and longitudinal follow-ups to validate these findings.

In conclusion, this study provides robust evidence supporting the use of pancreatic enzymes, particularly elastase, as potential biomarkers for early CKD detection. Given their high diagnostic accuracy and significant correlation with renal function decline, pancreatic enzyme assessments may serve as valuable, non-invasive tools in clinical nephrology. Further research is warranted to refine diagnostic thresholds and evaluate their prognostic value in CKD progression.

## Conclusion

This study has the potential role of pancreatic enzymes, particularly elastase, as early biomarkers for CKD detection. The significant elevation of these enzymes in CKD patients and their strong inverse correlation with eGFR suggest that they could serve as non-invasive diagnostic tools. Among the pancreatic enzymes evaluated, elastase demonstrated the highest diagnostic accuracy, highlighting its potential clinical utility. However, further research is needed to establish standardized diagnostic thresholds and evaluate the long-term prognostic value of pancreatic enzyme levels in CKD progression. Addressing current limitations, including variability in laboratory methods and confounding comorbidities, will be crucial for integrating these biomarkers into routine clinical practice. Ultimately, incorporating pancreatic enzyme assessments could enhance early detection and management of CKD, improving patient outcomes.

## References


1. Munguía-Miranda C, Paniagua-Sierra J. Biomarkers in Chronic Kidney Disease. Rev Med Inst Mex Seguro Soc. 2017;55 Suppl 2:S143-50.
2. Mishra S, Manju M, Rajendran S, Pavithra M. Serum Liver and Pancreatic Enzymes in Chronic Kidney Disease with and without End-stage Renal Disease: A Comparative Study. Indian J Med Biochem. 2019. doi:10.5005/JP-JOURNALS-10054-0087.
3. Mahawar S, Thadani D, Jakhalia AL, Chowdhry V, Makwana A. Evaluation of Serum Lipase Level in Non-Diabetic Chronic Kidney Disease Patients. Int J Adv Res. 2019. doi:10.21474/ijar01/10042.
4. Kaphalia B. Early Biomarkers of Acute and Chronic Pancreatitis. Biomarkers in Toxicology. 2019. doi:10.1016/B978-0-12-814655-2.00019-0.
5. Vilà-Quintana L, Fort E, Pardo L, et al. Exploring the Associations of Inflammatory and Oxidative Stress Biomarkers with Pancreatic Diseases: An Observational and Mendelian Randomisation Study. J Clin Med. 2024. doi:10.3390/jcm13082247.
6. Pal A, Mandal L. Serum Amylase in Patients of Chronic Kidney Disease Stage Three to Stage Five. Birat J Health Sci. 2018;3(2):403-7. doi:10.3126/BJHS.V3I2.20934.
7. Ross JJ, Wasserfall C, Bacher RL, et al. Exocrine Pancreatic Enzymes Are a Serological Biomarker for Type 1 Diabetes Staging and Pancreas Size. Diabetes. 2021;70:944-54. doi:10.2337/db20-0995.
8. Goldsworthy M, Purssell H, Al-Omari D, et al. Novel Biomarkers for the Diagnosis of Chronic Pancreatitis: An Exploratory Case-Control Study. Br J Surg. 2023. doi:10.1093/bjs/znad258.460.
9. Mizdrak M, Kumrić M, Kurir T, Božić J. Emerging Biomarkers for Early Detection of Chronic Kidney Disease. J Pers Med. 2022;12. doi:10.3390/jpm12040548.
10. Elgamal R, Melton RL, Chiou J, et al. Circulating Pancreatic Enzyme Levels Are a Causal Biomarker of Type 1 Diabetes. medRxiv. 2024. doi:10.1101/2024.08.08.24311619.
11. Mishra S, Manju M, Rajendran S, Pavithra M. Serum Liver and Pancreatic Enzymes in Chronic Kidney Disease. Indian J Med Biochem. 2019. doi:10.5005/jp-journals-10054-0087.
12. Mahawar S, Thadani D, Jakhalia AL, Chowdhry V, Makwana A. Evaluation of Serum Lipase Level in CKD. Int J Adv Res. 2019. doi:10.21474/ijar01/10042.
13. Pal A, Mandal L. Serum Amylase in CKD Stage 3-5. Birat J Health Sci. 2018. doi:10.3126/BJHS.V3I2.20934.
14. Ross JJ, Wasserfall C, Bacher RL, et al. Pancreatic Enzymes and Type 1 Diabetes. Diabetes. 2021. doi:10.2337/db20-0995.
15. Goldsworthy M, Purssell H, Al-Omari D, et al. Biomarkers for Chronic Pancreatitis. Br J Surg. 2023. doi:10.1093/bjs/znad258.460.