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Serine Protease in Patients with Renal Failure are Relevant to Their Demography

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Abstract

Serine proteases, a class of enzymes that play physiological role in digestion, blood coagulation, and immune response We sought to find the relation of serine proteases and level changes based on demography in patients with kidney failure compared to a control group. By evaluating 160 samples, comprising 80 from individuals with renal failure and 80 from healthy controls, the researchers observed a significant elevation in serine protease activity among kidney failure patients (274.38 ± 1.55 U/L) relative to the control group (173.78 ±1.49 U/L). Importantly, this enzyme's activity was unaffected by sex or smoking, though body mass index demonstrated age-related variability across both cohorts. These comprehensive findings underscore the profound metabolic disruptions inherent to kidney failure while providing pivotal insights into enzyme activities and mineral imbalances associated with this condition.

Keywords: Renal Failure; Serine Protease; Age; Sex; BMI

Introduction

Serine proteases are a class of enzymes that play a crucial role in various physiological processes, including digestion, blood coagulation, and immune response [1]. These enzymes are responsible for breaking down proteins into smaller peptides and amino acids, and they are essential for maintaining the balance of protein levels in the body [2]. However, when the activity of serine proteases is dysregulated, it can lead to various diseases, including chronic kidney disease (CKD) [3]. CKD is a progressive condition in which the kidneys gradually lose their function over time. This disease is characterized by a gradual decline in kidney function, leading to the accumulation of waste products and toxins in the body [4]. The two most common causes of CKD are diabetes and hypertension, but other factors such as genetic predisposition, autoimmune diseases, and infections can also contribute to its development [5]. Serine proteases have been implicated in the pathogenesis of CKD [3]. Studies have shown that increased activity of these enzymes can lead to the destruction of kidney tissue, resulting in a decline in kidney function [3,6]. This is because serine proteases can break down the extracellular matrix, a network of proteins and carbohydrates that provide structural support to the kidney tissue [6]. As a result, the kidney tissue becomes damaged, and its function is impaired. Moreover, serine proteases have also been linked to the development of fibrosis in the kidneys, which is a hallmark of CKD [3]. Fibrosis is the excessive accumulation of scar tissue in the kidneys, which disrupts their normal function. This process is initiated by the activation of certain signaling pathways that promote the production of extracellular matrix proteins [7]. Serine

proteases have been found to be involved in the activation of these pathways, leading to the progression of fibrosis in the kidneys [1]. In addition to their role in the pathogenesis of CKD, serine proteases have also been identified as potential biomarkers for the disease [3]. Biomarkers are measurable indicators of disease activity, and they can be used for diagnosis, prognosis, and monitoring of treatment response. Studies have shown that the levels of certain serine proteases, such as plasminogen activator inhibitor-1 (PAI-1) and tissue-type plasminogen activator (tPA), are elevated in patients with CKD [8-10]. These enzymes have been suggested to be useful biomarkers for predicting the progression of the disease and identifying patients at risk for developing CKD. The present study sought to find changes in levels of serine protease in patient with CKD based on demographic parameters.

Materials and Methods

Samples: The study was conducted on human blood serum samples and samples were collected for
the period from January 2022 to February 2022 in cooperation with Ibn Sina Hospital and Al-Salam Hospital in the Dialysis Department.
Control group: (80) blood samples were collected from apparently healthy persons, including (46)
males and (36) females, aged between (32-61) years.
Patient group: (80) blood samples were collected for people with kidney failure diseases, and
included (40) males and (40) females, and their condition was diagnosed by doctors specializing in nephrology and urology in cooperation with Al-Salam Hospital and the Mosul Center for Nephrology and Surgery, their ages ranged between (34-69) years.
Blood samples collection: blood samples were collected after sterilizing the area with Heptin,
where 8 ml of venous blood was withdrawn for the control group and the group of kidney failure patients and placed in plastic tubes and then left to coagulate at a temperature of (37°C), then a centrifugal of blood was conducted for a period of (20 min at a speed of (4000xg) to obtain blood serum.
Materials: In this study, several ready-made tests (standard Kit) from the French company (Biolabo)
were used to measure the concentration of serine protease. The procedure was conducted as per manufacturer instructions.

Results

The study comparing the effectiveness of serine protease in blood serum between patients with renal failure and healthy controls across three age groups reveals striking differences in enzyme activity. Statistical analysis demonstrated a very high significant increase ($P \leq 0.001$) in serine protease levels among renal failure patients compared to the control group, regardless of age. Specifically, in the first age group (≤45 years), renal failure patients exhibited an average serine protease activity of 269.27±2.01 U/L, significantly higher than the control group's 155.56±2.47 U/L. Similarly, for individuals aged 45-55 years, patients showed an enzyme activity level of 278.71±3.16 U/L, contrasted with the control's 173.76±0.55 U/L-a substantial elevation that underscores the marked enzymatic dysregulation associated with renal impairment ($P \leq 0.001$). In the oldest cohort (≥55 years), this trend continued, with patients recording a mean serine protease activity of 282.43±2.28 U/L against the control group's 190.72±1.20 U/L, further solidifying the pattern of heightened enzymatic activity correlating with disease presence and progression ($P \leq 0.001$). These findings suggest that elevated serine protease activity may be closely linked to renal pathology and could serve as a valuable biomarker for monitoring kidney health deterioration across different age (Figure 1).

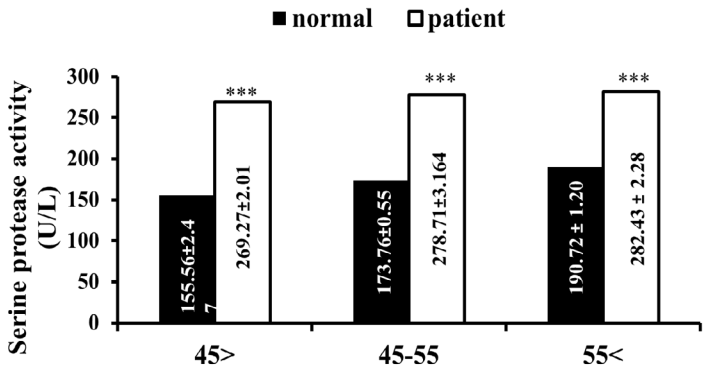

Figure 1: Serine protease activity in renal failure patients versus control at different age group. Data expressed as mean±SD (n=80 each group).

The comparative analysis of serine protease activity in the serum between renal failure patients and control groups revealed a striking disparity contingent on sex, demonstrating significant elevation in the patient cohort. In males with renal failure, serine protease activity reached 271.57 ± 2.05 U/L, while females exhibited even higher levels at 277.20 ± 2.27 U/L (P ≤ 0.001). These measurements starkly contrast with those in the control group, where male participants had an activity level of 179.54 ± 1.77 U/L and females recorded levels at 168.35 ± 2.16 U/L, respectively (Figure 2).

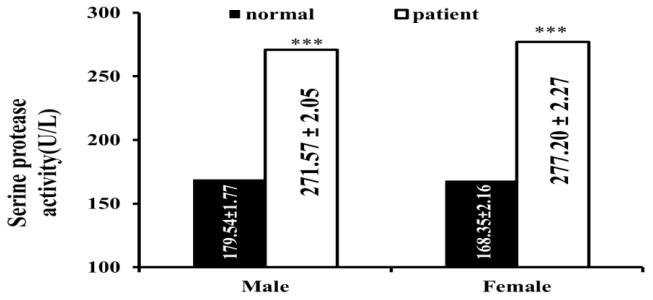

Figure 2: Serine protease activity in renal failure patients versus control based on gendre. Data expressed as mean±SD (n=80 each group.

The results demonstrated a highly significant increase in serine protease activity levels in the serum of both smokers and non-smokers diagnosed with renal failure compared to their respective control groups. For smokers, the serine protease activity was reported at 271.78 ± 2.42 U/L for those with renal failure and 178.71 ± 1.61 U/L for the control group, marking a substantial elevation at a probability level of P ≤ 0.001. Similarly, non-smokers exhibited an even greater serine protease activity, with values recorded at 276.12 ± 2.0 U/L in the renal failure group and 170.4 ± 2.43 U/L in the control group, also indicating a significant rise at P ≤ 0.001 (Figure 3).

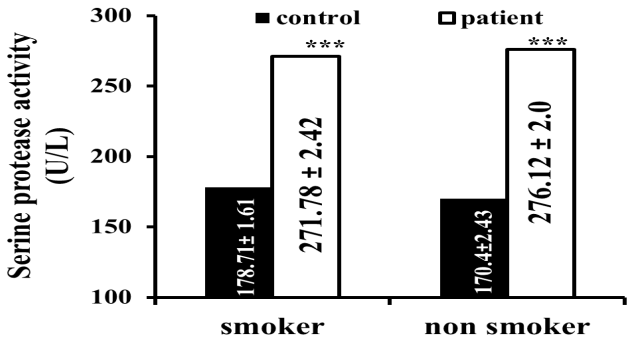

Figure 3: Serine protease activity in renal failure patients versus control based on smoking status. Data expressed as mean±SD (n=80 each group).

The data illustrated a statistically significant escalation in the serine protease activity within blood serum among renal failure patients, relative to healthy individuals, when analyzed according to body mass index (BMI) categories. At a stringent probability level of P≤0.001, findings reveal that for individuals classified within the normal weight range (18.5-24.9 BMI), renal failure patients exhibit markedly higher serine protease levels at 268.05±1.17 U/L, compared to their healthy counterparts who present levels of 170.27±1.88 U/L. This pattern intensifies among those in the overweight category (25-29.9 BMI), where patients with renal failure demonstrate an even more pronounced increase in serine protease activity at 293.40±1.42 U/L, contrasted against 173.91±2.61 U/L observed in healthy subjects within the same BMI range (Figure 4).

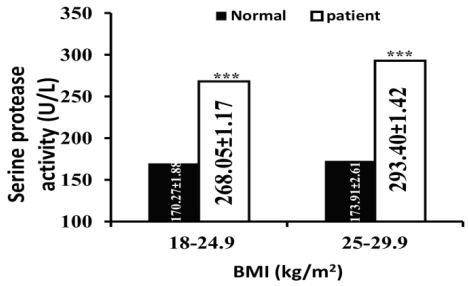

Figure 4: Serine protease activity in renal failure patients versus control based on BMI. Data expressed as mean±SD (n=80 each group).

Discussion

The findings of the study suggest that there is a significant increase in serine protease levels in patients with renal failure compared to healthy individuals. This increase was observed in all three age groups (≤45 years, 45-55 years, and ≥55 years) and was found to be highly significant with a significance level of P ≤ 0.001. The results of this study raise important questions about the role of serine protease in the pathophysiology of renal failure. It is known that serine protease is involved in various physiological processes, including blood clotting, immune response, and tissue remodeling. However, its specific role in renal failure has not been fully understood. One possible explanation for the elevated levels of serine protease in patients with renal failure is that it is a response to the underlying condition.

It is possible that the increase in serine protease levels is a result of the body's attempt to repair and regenerate damaged tissues in the kidneys. Another possibility is that the elevated levels of serine protease may contribute to the progression of renal failure. Studies have shown that this enzyme can

promote inflammation and tissue damage, which are key processes in the development of renal failure. Therefore, the increase in serine protease levels may exacerbate the existing damage in the kidneys and contribute to the deterioration of renal function. The age-specific differences in serine protease levels also warrant further investigation. The study found that the increase in enzyme activity was more pronounced in older individuals (≥55 years) compared to younger ones (≤45 years). This could be due to the fact that as we age, our bodies become less efficient in repairing and regenerating damaged tissues, leading to a higher accumulation of serine protease. It is also worth noting that the study only evaluated serine protease levels in the blood serum of patients with renal failure. This may not accurately reflect the levels of this enzyme in the kidneys, where it could have a more direct impact on renal function.

Future studies should consider measuring serine protease levels in the kidneys to gain a better understanding of its role in renal failure. The comparative analysis of serine protease activity in the serum between renal failure patients and control groups has revealed a significant difference in the levels of this enzyme between males and females. The study found that in both the patient and the control group, females had higher levels of serine protease activity compared to males. However, the difference was even more pronounced in the renal failure patients, with females exhibiting significantly higher levels than males. This finding highlights the potential role of sex in the development and progression of renal failure. It suggests that there may be underlying biological factors that contribute to the differences in serine protease activity between males and females, and that these factors may have a significant impact on the disease.

One possible explanation for these differences could be the hormonal differences between males and females. Estrogen, a female hormone, has been shown to have a protective effect on the kidneys, while testosterone, a male hormone, has been linked to kidney damage. This could potentially explain why females with renal failure have higher levels of serine protease activity compared to males. Another factor that could contribute to these differences is the difference in body composition between males and females. It is well-known that women generally have a higher percentage of body fat compared to men. This could affect the distribution and metabolism of drugs and toxins in the body, potentially leading to higher levels of serine protease activity in females with renal failure. It is also important to consider the potential impact of lifestyle and environmental factors on serine protease activity. It is possible that females with renal failure may be exposed to certain risk factors, such as certain medications or toxins, that could contribute to the elevated levels of this enzyme.

The results reported a significant increase in serine protease activity in both groups, indicating a potential link between smoking and renal failure. The study's findings are consistent with previous research that has linked smoking to adverse effects on kidney function. Smoking has been shown to increase oxidative stress and inflammation in the body, which can contribute to the development and progression of renal failure. The elevated serine protease activity observed in both smokers and non-smokers with renal failure further supports this connection. It is also worth noting that the non-smokers in the study exhibited higher serine protease activity levels compared to the smokers. This may be due to the fact that non-smokers with renal failure may have other underlying health conditions that could contribute to increased serine protease activity [11-14].

The results of this study show a significant increase in serine protease activity in renal failure patients compared to healthy individuals. This increase is even more pronounced in patients who fall within the overweight category, as opposed to those in the normal weight range. The results highlight the impact of BMI on serine protease activity. In this study, the increase in serine protease activity was more pronounced in overweight individuals, suggesting that excess body fat may play a role in this phenomenon. This finding is consistent with previous research that has linked obesity to increased inflammation and altered enzyme activity [15-17]. It is worth noting that the study's findings are based on a small sample size and may not be representative of the entire population. Further research with a larger and more diverse sample is needed to confirm these results. Additionally, the study only focused on serine protease activity and did not consider other factors that could potentially influence enzyme levels, such as medications or diet.

Conclusion

In conclusion, the presence of Serine Protease in patients with renal failure is highly relevant to their demographic characteristics. This enzyme has been shown to be elevated in individuals with renal failure, especially in older adults, female, smokers and overweight and those with comorbidities such as diabetes and hypertension.

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