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Beta-trace protein (BTP): A Marker of Renal Dysfunction in Essential Hypertensive Patients

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ABSTRACT

Background: Hypertension (HTN) is a major cause of chronic kidney disease (CKD), leading to renal damage known as hypertensive nephrosclerosis. Beta-trace protein (BTP), or lipocalin-type prostaglandin D synthase, has emerged as a sensitive marker of glomerular filtration rate (GFR), outperforming creatinine in early renal impairment.

Aim: To evaluate serum and urinary BTP as potential indicators of early kidney injury in essential hypertension.

Patients and methods: This cross-sectional clinical study was conducted at the Internal Medicine Department, Menoufia University Hospital, Egypt, in accordance with Institutional Medical Ethical standards. A total of 40 participants were enrolled, including 30 patients with essential hypertension and 10 healthy individuals serving as controls. Informed consent will be obtained from all participants following approval by the Local Ethical Committee. The study was scheduled to commence in 2020.

Aims: To investigate the relationship between hypertension and renal dysfunction.

Results: Serum BTP (cut-off point=3025) and urinary BTP (cut-off point=825) had excellent diagnostic accuracy for the condition. Serum BTP demonstrated 95.8% sensitivity and specificity with an AUC of 0.997 (95% CI 0.990–1.00), while urinary BTP showed 91.7% sensitivity and specificity with an AUC of 0.986 (95% CI 0.962–1.00). Both are highly significant ($p < 0.001$), with serum BTP showing slightly superior performance.

Conclusion: Beta-trace protein is a valuable, non-invasive biomarker for early renal dysfunction in hypertension and may complement traditional renal tests. Larger longitudinal studies are needed to confirm its prognostic utility and establish reference ranges.

Keywords: CKD, ESRD, RRT, BTP, serum L-PGDS, PGD2, HTN.

INTRODUCTION

Chronic kidney disease (CKD) is defined as an irreversible state of kidney damage that carries the risk of progression to end-stage renal disease (ESRD), a critical health condition. In the United States, the total population currently living with ESRD exceeds 800,000 individuals, among these patients, approximately 68% are reliant upon regular dialysis treatments, while the remaining 32% have received a kidney transplant [(1)].

Despite its severe consequences, CKD is a highly prevalent medical condition within the adult population; however, a significant proportion of these affected adults remain unaware of their diagnosis, and despite the documented severe health consequences associated with CKD, the condition represents a substantially prevalent medical issue across the adult population; however, a critical challenge in public health remains the fact that a significant proportion of the affected adults are currently unaware of their own diagnosis [(2)]. This lack of awareness poses a major barrier to timely intervention and management, which are crucial factors for slowing disease progression and mitigating the risk of end-stage renal disease [(2)].

ESRD is a devastating disorder with high mortality and morbidity, but elevated risks are evident even in early CKD stages. Renal transplantation improves survival and reduces morbidity, though post-transplant patients still carry higher risks of disease and early mortality compared to age-matched general population [(3)]. Hypertension is one of the major causes of CKD and progression to ESRD. The relative risk of serious renal damage in uncomplicated essential hypertension is lower than for cardiovascular complications, but because hypertension is highly prevalent, it remains a leading cause of ESRD, especially in Black populations [(3)]. Over the last decades, recognition has increased that hypertension-induced renal damage is broader than classical nephrosclerosis; hypertension often contributes substantially to progression of CKD when coexisting with other renal insults [(3,4)].

Beta-trace protein (BTP), which is also known by its biochemical name lipocalin-type prostaglandin D2 synthase (L-PGDS), is categorized as a low molecular weight glycoprotein. This protein is freely filtered from the blood by the glomerulus in the kidney and is then largely excreted through the renal pathway. Due to its favorable biochemical characteristics—specifically its low molecular mass, its relatively constant production rate within the body, and its overall stability—BTP has been extensively investigated in clinical research as a potential endogenous marker of glomerular filtration

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rate (GFR) [3]. This makes it a compelling candidate for assessing kidney function [3].

Several studies have examined the behaviour of serum L-PGDS/BTP in renal dysfunction; elevated levels are seen in chronic kidney disease, likely reflecting impaired filtration [4]. In cardiovascular research, L-PGDS/BTP expression has been detected in vascular smooth muscle cells with synthetic phenotypes, in atherosclerotic intima, and in plaques of coronary arteries with severe stenosis [5].

L-PGDS is bifunctional: it acts as an enzyme synthesizing prostaglandin D_2 (PGD_2) and as a carrier (lipocalin) for small lipophilic molecules such as retinol [3]. Prostaglandin D_2 has roles in neurophysiological functions (e.g., thermoregulation, hormone release, sleep–wake cycle). In renal physiology, intrarenal infusion of PGD_2 has been shown in older experiments to increase renal blood flow, urine output, creatinine clearance, and sodium/potassium excretion in a dose-dependent manner. Given its properties, BTP remains of interest as a filtering marker, though more recent comparative studies suggest that combinations of biomarkers (creatinine, cystatin C, BTP, β2-microglobulin) may have better accuracy than any single marker [3].

Aims of the study:

The central objective of this investigation is to empirically study the concentrations of Beta-Trace Protein (BTP) in both urine and serum samples. This analysis was conducted specifically to evaluate the utility of BTP levels as a potential biomarker for the presence of renal dysfunction within a patient population diagnosed with essential hypertension. The research was designed to determine if deviations in BTP levels could reliably signal impaired kidney function in this high-risk group.

PATIENTS AND METHODS

Study design and patient setting:

This was a cross-sectional clinical study executed at the Internal Medicine Department, Menoufia University Hospital, Egypt. The investigation was conducted over a significant period, extending from September 2020 till March 2024. and was carried out in full compliance with all prevailing institutional ethical standards. The final study cohort comprised a total of 40 participants. This total was divided into two distinct groups: 30 patients who had a confirmed diagnosis of essential hypertension and 10 healthy individuals who served as the designated controls. Prior to enrollment, informed consent was successfully obtained from every subject in accordance with the established guidelines of the Local Ethical Committee.

Study population and grouping:

The total cohort enrolled in this research consisted of 40 participants, which included 30 patients with essential hypertension and 10 healthy control subjects. For the purpose of comparative analysis, this study population was systematically stratified into three distinct groups: Group 1 served as the non-hypertensive, healthy control cohort and comprised 10 normal individuals, Group 2 was made up of 15 patients diagnosed with essential hypertension (defined by a blood pressure of 140/90 mmHg or higher) who concurrently demonstrated normal kidney function, and Group 3 included the remaining 15 patients with essential hypertension who also presented with impaired kidney function. This tripartite division allowed for the comparison of BTP levels across healthy individuals, and hypertensive patients with and without evidence of renal dysfunction.

Diagnostic criteria of patients:

Hypertension was diagnosed according to the JNC 8 classification [6]. Essential hypertension was confirmed in patients with a history of elevated blood pressure or those receiving antihypertensive treatment, with repeated BP ≥140/90 mmHg on subsequent visits. Hypertensive nephropathy was diagnosed based on the criteria described by **Izzo *et al.* [7],** including primary hypertension persisting for more than five years, presence of mild-to-moderate proteinuria, benign urinary sediment, retinal arteriosclerosis, and exclusion of other primary or secondary renal diseases.

Patients' selection criteria:

This study included adult patients (>18 years) of both sexes who had been diagnosed with essential hypertension for a duration of at least five years. Patients with diabetes mellitus, secondary hypertension, primary renal diseases, acute kidney injury, autoimmune diseases, post-obstructive nephropathy, malignancy, or pregnancy were excluded. Individuals receiving recent or concurrent nephrotoxic medications were also excluded from participation to eliminate potential confounding factors,

Sample size estimation:

Based on previous studies showing a strong correlation ($r = 0.65$) between serum BTP and renal function parameters in hypertensive patients, a minimum of 36 participants was required to achieve a power of 80% and a significance level of 0.05. To ensure adequate representation and account for potential data loss, 40 subjects were included (30 hypertensive and 10 healthy controls).

All patients were subjected to the following:

All participants were subjected to thorough medical history taking and complete physical examination with particular emphasis on blood pressure, weight, height, and body mass index (BMI). Routine laboratory investigations included complete blood count (CBC), fasting and postprandial blood glucose levels, plasma lipid profile (cholesterol, triglycerides, LDL, and HDL), renal function tests

(serum creatinine, blood urea nitrogen, sodium, and potassium), serum uric acid, and urinalysis. The estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease (MDRD) formula [8], GFR = 170 × (serum creatinine concentration) ^–0.999 × (age)^ –0.176 × 0.762 (if female) × 1.180 (if black) × (blood urea nitrogen concentration) ^–0.17 × (serum albumin concentration) ^–0.318. Liver function tests included serum albumin, prothrombin time and INR, ALT, AST, and total and direct bilirubin. Additional assessments comprised 12-lead resting electrocardiography (ECG), pelvi-abdominal ultrasonography, and fundus examination.

Special investigations included measurement of the urinary albumin-to-creatinine ratio (UACR) and detection of beta-trace protein (BTP) levels in both serum and urine using an enzyme-linked immunosorbent assay (ELISA). Blood pressure was measured according to the European Society of Hypertension guidelines [9]. For blood sampling, two milliliters of venous blood were collected under aseptic conditions and transferred into plain tubes for BTP determination by ELISA. The urinary albumin/creatinine ratio was obtained from a spot urine sample, where the upper normal limits were defined as 10 mg/g for men and 15 mg/g for women [8]. Measurement of BTP concentrations in serum and urine was performed using the Human PGD2S (Prostaglandin D2 Synthase) ELISA Kit.

Diagnosis of hypertension and hypertensive nephropathy:

The diagnosis of hypertension was established according to the Joint National Committee (JNC 8) guidelines [6]. Blood pressure (BP) was classified as Normal: Systolic BP <120 mmHg and diastolic BP <80 mmHg, Prehypertension: Systolic BP 120–139 mmHg or diastolic BP 80–89 mmHg, Stage 1 Hypertension: Systolic BP 140–159 mmHg or diastolic BP 90–99 mmHg and Stage 2 Hypertension: Systolic BP ≥160 mmHg or diastolic BP ≥100 mmHg. Essential hypertension was diagnosed in patients with a known history of elevated blood pressure, use of antihypertensive medications, or persistent BP readings ≥140/90 mmHg on a subsequent visit one to four weeks after the initial measurement [10].

The diagnosis of hypertensive nephropathy was based on the criteria proposed by **Izzo *et al.* [7],** which included Presence of primary hypertension for more than five years prior to the onset of proteinuria, persistent mild-to-moderate proteinuria with benign urinary sediment on microscopic examination, evidence of retinal arteriosclerosis or arteriosclerotic retinal changes, exclusion of primary and secondary renal diseases. Additional supportive diagnostic findings include a history of hypertensive, left ventricular hypertrophy, coronary heart disease, heart failure, cerebrovascular atherosclerosis, hyperuricemia, or renal tubular dysfunction preceding renal impairment, as well as slow progression of renal damage.

Ethical consideration:

The ethical framework for this investigation was established and upheld through several critical steps. **The entire study protocol underwent a thorough review and subsequently received formal approval from the Local Ethical Committee of Menoufia University Hospital. All experimental and data collection procedures were executed in strict adherence to the ethical standards set forth by the Institutional Research Committee. Furthermore, the study fully complied with the foundational ethical principles governing medical research involving human subjects, as outlined in the Declaration of Helsinki.** Prior to their formal enrollment in the research, written informed consent was secured from every participant. This consent was obtained only after the subjects received a full and comprehensive explanation detailing the study's objectives, the specific procedures they would undergo, and any potential risks involved. To ensure the rights and autonomy of the participants were protected, they were given explicit assurances regarding the confidentiality of their data, were informed of their inherent right to withdraw from the study at any point without experiencing any adverse consequences, and were guaranteed that all information collected would be utilized solely for scientific purposes.

Statistical analysis

Data were coded, tabulated, and analyzed using the Statistical Package for Social Sciences (SPSS) version 26.0 (IBM, Chicago, USA). Descriptive statistics were expressed as number and percentage for qualitative variables, and as mean ± standard deviation (SD) or median (interquartile range, IQR) for quantitative variables. Analytical statistics included the Chi-squared test (χ^2) for categorical data, One-way ANOVA for comparison among normally distributed quantitative variables, and the Kruskal–Walli's test for non-parametric data. Pearson's correlation coefficient was used to assess relationships between continuous variables. Normality was tested using the Shapiro–Wilk test, assuming normal distribution at $p > 0.05$, and statistical significance was set at $p < 0.05$.

RESULTS

In the current study, there was a statistically significant difference between the 3 groups regarding age, as group III had the highest age and group I had the youngest age (p<0.001). BMI was highest among group II and lowest among group III, with a statistically significant difference (p<0.001). Blood pressure, either systolic or diastolic, was higher in groups II and III, with a statistically significant difference (p<0.001) **(Table 1).**

Table (1): Demographics and baseline characteristics of the studied groups.

The variables	Group I (N=24)	Group II (N=24)	Group III (N=24)	Test	P-value	Post hoc test
Age (in years) Mean ±SD Range	 58.3±4.3 45 – 65	 57.8±8.7 47 – 76	 66.5±9.2 54 – 83	F=9.73	<0.001**	P1=1 P2=0.001* P3=0.001*
Sex (n (%) Male Female	 13 (54.2) 11 (45.8)	 11 (45.8) 13 (54.2)	14 (58.3) 10 (41.7)	$\chi 2$= 0.780	0.677	
BMI (kg/m^2) Mean ±SD Range	 23.9±1.1 22.7 – 26.5	 25.4±1.1 23.5 – 27.1	 22.9±0.6 21.8 – 24.1	F=40.77	<0.001**	P1=<0.001** P2=0.004* P3=<0.001**
Systolic Bp (mmHg) Mean ±SD Range	 119.6±3.9 110 – 125	 146.0±4.9 135 – 154	 151.1±3.1 148 – 162	F=409.97	<0.001**	P1=<0.001** P2=<0.001** P3=<0.001**
Diastolic Bp (mmHg) Mean ±SD Range	 78.6±2.9 70 – 82	 94.5±4.6 82 – 102	 97.1±3.7 92 – 105	F=166.17	<0.001**	P1=<0.001** P2=<0.001** P3=0.071

SD: Standard deviation, **χ2:** Chi-squared test, **F:** One-way ANOVA test, **BMI:** Body mass index, ***:** Statistically significant, ****:** Statistically highly significant, **P1:** Comparison between group I and group II. **P2:** Comparison between group I and group III, **P3:** Comparison between group II and group III

Results of the present study showed that Hemoglobin had the lowest values among group III, with statistically significant difference when compared to group I or II *(p=0.001; 0.001).* White blood cells had the lowest values in group I, with statistically significant differences when compared to group I or II *(p=0.004; 0.002).* Platelets had the highest values in group II, with a statistically significant difference when compared to group I or III *(p=0.004; 0.005).* Regarding the renal function, Renal Function: Group III exhibited significantly impaired renal markers elevated serum creatinine and urea, reduced eGFR, and markedly increased urinary albumin/creatinine ratio (P<0.001) suggesting advanced kidney dysfunction. Regarding uric acid, Group III showed hyperuricemia (P2, P3<0.001), often associated with renal impairment and cardiovascular risk. Lipid profile components (Cholesterol, TGs, LDL, HDL) and electrolytes (Na, K) did not differ significantly among groups, suggesting these parameters may not be primary discriminators in this study. *Additionally*, that Serum and urinary BTP were higher in groups II and III than in group I, with statistically significant differences. Serum and urinary BTP were higher in group III than in group II, with statistically significant differences (p <0.001) **(Table 2).**

Table (2): Comparison among the groups studied regarding the Laboratory data.

The variables	Group I (N=24)	Group II (N=24)	Group III (N=24)	Test	P-value	Post hoc test
Hgb (g/dL) Mean ±SD	12.6±1.3	12.9±0.9	10.9±0.6	**F= 26.15**	**<0.001****	P1=1 P2=<0.001** P3=<0.001**
WBC (10^3/L) Mean ±SD	6.0±1.4	7.5±1.6	7.6±1.4	**F= 7.96**	**0.001***	P1=0.004* P2=0.002* P3=1
PLT (10^9/L) Mean ±SD	252.6±49.5	312.5±74.5	253.8±59.7	**F= 7.29**	**0.001***	P1=0.004* P2=1 P3=0.005*
Cholesterol (mg/dL) Mean ±SD	130.2±11.9	128.6±11.5	133.5±10.2	**F= 1.18**	**0.314**	---
TGs (mg/dL) Mean ±SD	92.3±6.3	92.0±7.1	92.3±5.8	**F= 0.01**	**0.990**	---
LDL (mg/dL) Mean ±SD	78.0±7.9	77.3±7.9	74.2±6.4	**F= 1.78**	**0.177**	---
HDL (mg/dL) Mean ±SD	41.9±4.6	41.9±3.5	42.5±3.6	**F= 0.142**	**0.868**	---
S. creatinine (mg/dL) Mean ±SD	0.8±0.1	0.9±0.1	2.0±0.5	**F= 128.65**	**<0.001**	P1=1 P2=<0.001** P3=<0.001**
S. urea (mg/dL) Mean ±SD	33.4±5.7	25.7±7.4	86.5±16.5	**F= 219.87**	**<0.001**	P1=0.052 P2=<0.001** P3=<0.001**
Urinary Alb/cr ratio Mean ±SD	9.2±0.9	82.4±79.9	1472.5±93.3	**K= 60.83**	**<0.001**	P1=0.165 P2=<0.001** P3=<0.001**
eGFR Mean ±SD	108.7±5.9	93.8±7.4	46.1±5.8	**F= 618.81**	**<0.001**	P1=<0.001** P2=<0.001** P3=<0.001**
Uric acid (mg/dL) Mean ±SD	5.2±0.9	5.6±0.7	7.2±0.5	**F= 54.98**	**<0.001**	P1=0.264 P2=<0.001** P3=<0.001**
Na (mmol/L) Mean ±SD	137.2±2.1	138.6±1.9	138.1±2.5	**F= 2.67**	**0.072**	NS
K (mmol/L) Mean ±SD	3.9±0.3	4.1±0.5	4.1±0.4	**F= 2.62**	**0.080**	NS
Serum BTP Mean ±SD	281.2±39.5	1739.2±494.1	3705.8±396.0	F= 528.25	**<0.001**	P1=<0.001** P2=<0.001** P3=<0.001**
Urine BTP Mean ±SD	187.8±27.8	672.6±183.9	1108.5±188.6	F= 217.64	**=<0.001**	P1=<0.001** P2=<0.001** P3=<0.001**

SD: Standard deviation, **χ2:** Chi-squared test, **F:** One-way ANOVA test, **BMI:** Body mass index, **K:** Kruskal-Wallis, ***:** Statistically significant, ****:** Statistically highly significant, **P1:** Comparison between group I and group II, **P2:** Comparison between group I and group III, **P3:** Comparison between group II and group III.NS:non significant

The correlation analysis reveals significant negative associations between serum eGFR and certain demographic and clinical variables, particularly in Group III, where the relationships are stronger. In both Group II and Group III, age is negatively correlated with eGFR (r=-0.475, p=0.019 and r = -0.674, p<0.001, respectively), indicating that renal function declines with increasing age. Urinary albumin-to-creatinine ratio also shows a significant negative correlation with eGFR in both groups (r =-0.466, p=0.022 for Group II and r = -0.548, p=0.006 for Group III), suggesting that higher albuminuria is associated with poorer kidney function. Notably, in Group III, systolic and diastolic blood pressures are significantly inversely correlated with eGFR (r =-0.591, p=0.002 and r =-0.732, p <0.001), whereas such correlations are absent or weak in Group II. This implies that elevated blood pressure is more closely linked to decreased renal function in Group III. Also, serum BTP shows a significantly strong negative correlation with eGFR in both groups (r = -0.907, p.<0.00 for Group II and r = -0.981, p.<0.001 for Group III).In Addition, urinary BTP shows a significant strong negative correlation with eGFR in group II and moderate negative correlation in the group III (r =-0.907, p.<0.001 for Group II and r = -0.981, p.<0.001 for Group III) These findings highlight the important influence of age, blood pressure, and albuminuria on renal function decline, especially in the more advanced or affected group **(Table 3).**

Table (3): Pearson Correlation among serum eGFR and studied demographic data in groups II & III.

The variables	Group II		Group III	
	r	**P value**	**R**	**P value**
Age	-0.475	**0.019***	-0.674	**<0.001****
BMI	-0.103	0.633	0.192	0.368
Systolic Bp	0.230	0.280	-0.591	**0.002***
Diastolic Bp	-0.079	0.713	-0.732	**<0.001****
serum BTP	-0.907	**<0.001****	-0.981	**<0.001****
urinary BTP	-0.907	**<0.001****	-0.451	**0.027***
Urinary Alb/cr ratio	-0.466	**0.022***	-0.548	**0.006***

r= correlation coefficient

In the present study, serum BTP (cut-off point=3025) and urinary BTP (cut-off point=825) have excellent diagnostic accuracy for the condition among hypertensive patients (group II and III). Serum BTP demonstrated 95.8% sensitivity and specificity with an AUC of 0.997 (95% CI 0.990–1.00), while urinary BTP showed 91.7% sensitivity and specificity with an AUC of 0.986 (95% CI 0.962–1.00). Both are highly significant (p <0.001), with serum BTP showing slightly superior performance **(Figure 1).**

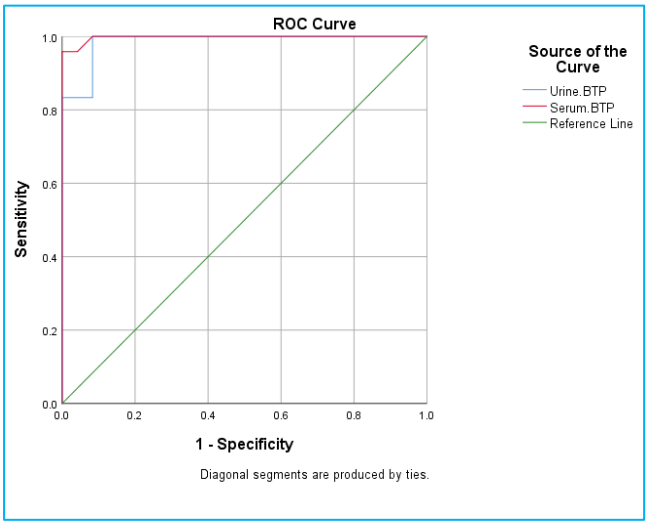

Figure (1): ROC curve of serum and urinary BTP among hypertensive patients (group II and III).

The current study shows excellent diagnostic performance for both serum BTP and urinary BTP, among the studied patients (group I and II). Serum BTP at a cut-off of 1290 achieved perfect discrimination with an AUC of 1.00, 91.7% sensitivity, and 100% specificity (p < 0.001). Urinary BTP at a cut-off of 216 also showed high accuracy with an AUC of 0.962, 91.7% sensitivity, and 87.5% specificity (p<0.001). Both markers demonstrate strong potential as reliable diagnostic tests **(Figure 2).**

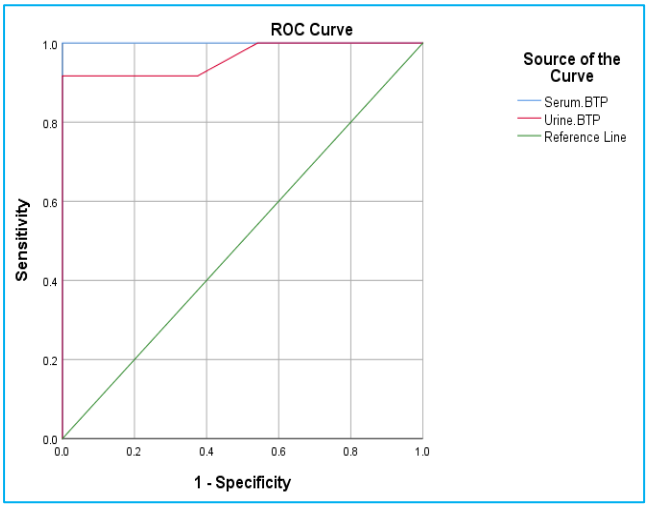

Figure (2): ROC curve of serum and urinary BTP among the studied groups (group I and II).

DISCUSSION

Global epidemiological studies indicate that hypertensive nephropathy accounts for a substantial proportion of end-stage renal disease, particularly in populations with suboptimal blood pressure control [(11)].

Early identification of renal dysfunction in hypertensive patients is vital to prevent irreversible nephropathy and associated cardiovascular risks. Conventional renal markers—serum creatinine, estimated GFR, and urinary albumin-to-creatinine ratio—remain the main diagnostic tools but have significant limitations. Serum creatinine is influenced by age, muscle mass, and dietary intake, and often remains within normal limits until substantial nephron loss occurs [12]. Albuminuria, though a reliable indicator of glomerular injury, may not appear in early hypertensive nephropathy, underscoring the need for more sensitive biomarkers [13].

Beta-trace protein (BTP), or lipocalin-type prostaglandin D synthase, has emerged as a promising renal biomarker. It is less influenced by non-renal factors such as muscle mass and sex and may allow earlier detection of renal dysfunction [14]. BTP has also been associated with cardiovascular and microvascular injury, reflecting shared mechanisms of endothelial dysfunction and inflammation [15].

In the present study, hypertensive patients with renal impairment showed significant biochemical evidence of renal deterioration, including increased serum creatinine, urea, and urinary albumin, with a parallel reduction in estimated GFR. These findings are consistent with the progressive nephrosclerosis characteristic of chronic hypertension. Comparable results were reported by **Hati *et al.*** [16], who demonstrated that both serum creatinine and urinary microalbumin increase with longer disease duration in essential hypertension. **Huang *et al.*** [17] further proposed that albuminuria is not merely a consequence but may also predict future hypertension, suggesting a bidirectional relationship between renal endothelial injury and elevated blood pressure.

Serum and urinary BTP levels in the current study were significantly higher among hypertensive patients, particularly those with impaired renal function, confirming its close relationship with renal deterioration. Similar findings were previously documented by **Hoffmann *et al.*** [18] and **Melegos *et al.*** [19], who observed markedly elevated serum BTP levels in patients with chronic kidney disorders compared to healthy controls. **Dajak *et al.*** [20] also demonstrated that serum BTP concentrations increase progressively with advancing chronic kidney disease stages, supporting its association with glomerular filtration rate. The reference range of 0.40–0.74 mg/L established by Poge ***et al.*** [21] provides a benchmark indicating that the elevated levels observed here signify true renal impairment rather than physiological variation.

The graded increase in BTP across the hypertensive groups mirrors the pattern reported by **Dajak *et al.*** [20], suggesting that BTP reflects not only glomerular filtration efficiency but also early tubular and vascular injury from sustained hypertension. Experimental work by **Hirawa *et al.*** [22] and clinical data by **Huang *et al.*** [17] support this mechanism, linking hypertension-induced microvascular damage to impaired clearance of low–molecular weight proteins such as BTP.

Beyond renal function, BTP is expressed in myocardial and vascular tissues [14,23] and correlates with cardiovascular risk. The Atherosclerosis Risk in Communities (ARIC) study demonstrated that BTP independently predicts cardiovascular disease [15]. Elevated BTP levels may thus reflect systemic vascular pathology rather than isolated renal dysfunction. However, **Elebidi *et al.*** [24] reported no significant difference in BTP levels between hypertensive and control groups. This discrepancy may stem from variations in sample size, disease stage, and duration of hypertension, as BTP elevation is more evident with prolonged vascular and renal injury.

Correlation analysis in the present study revealed strong negative associations between estimated GFR and several demographic and clinical parameters. In both hypertensive groups, renal function declined with advancing age, reflected by significant negative correlations between age and eGFR ($r = –0.475$, $p = 0.019$ in Group II; $r = –0.674$, $p < 0.001$ in Group III). These results confirm the well-established relationship between aging and progressive loss of renal function due to cumulative vascular and parenchymal injury. The stronger correlation observed in Group III suggests that age-related changes exacerbate hypertensive nephropathy. **Ma *et al.*** [13] similarly reported age as an independent predictor of reduced eGFR in a large Canadian cohort of over 340,000 adults, highlighting the additive effects of aging and hypertension on renal vulnerability.

The urinary albumin-to-creatinine ratio also showed a significant inverse correlation with eGFR in both hypertensive groups ($r = –0.466$, $p = 0.022$ for Group II; $r = –0.548$, $p = 0.006$ for Group III), indicating that increasing albuminuria accompanies declining renal function. **Grams *et al.*** [25] similarly found that both reduced eGFR and elevated albuminuria independently predict acute kidney injury and adverse renal outcomes. Together, these results reinforce the interdependence between glomerular and vascular injury in hypertensive renal disease.

Systolic and diastolic blood pressures showed significant negative correlations with eGFR in Group III ($r = –0.591$, $p = 0.002$ and $r = –0.732$, $p < 0.001$, respectively), suggesting a stronger detrimental effect of elevated blood pressure in advanced disease stages. In early hypertension (Group II), weaker correlations may reflect temporary preservation of renal autoregulation. Chronic elevation in blood pressure eventually leads to glomerular hypertension, arteriolar remodeling, and progressive nephrosclerosis. These findings are consistent with established pathophysiological models of hypertensive renal injury.

Serum creatinine remains the conventional marker for estimating glomerular filtration rate, but its

sensitivity in early disease is limited. As noted by **Herget *et al.* [12]**, creatinine levels are influenced by several non-renal factors and may not capture subtle renal impairment. This limitation highlights the need for complementary biomarkers such as BTP to improve early detection accuracy.

Receiver operating characteristic (ROC) analysis in this study demonstrated exceptional diagnostic precision for both serum and urinary BTP in differentiating healthy individuals, hypertensive patients with preserved renal function, and those with impaired renal function. Serum BTP consistently outperformed urinary BTP, exhibiting slightly higher sensitivity and specificity across all comparisons. These findings are consistent with **Dajak *et al.* [20]**, who reported AUC values between 0.917 and 0.983 for BTP in detecting reduced eGFR, and with **Donadio *et al.* [14]**, who demonstrated similar performance in urinary assays. Comparable results have been reported in other populations. **Nakayama *et al.* [26] and Vynckier *et al.* [27]** confirmed that both serum and urinary BTP retain high diagnostic accuracy for identifying reduced GFR, independent of age and sex. **Hebah *et al.* [28]** also observed strong diagnostic performance of BTP in diabetic patients, identifying a serum cut-off of 260 ng/mL that achieved an AUC of 0.848 with 80% sensitivity and specificity. Although their cohort differed etiologically, their results further support the broad applicability of BTP in detecting early renal dysfunction.

The near-perfect discrimination observed in the present study underscores BTP's reproducibility and robustness as a renal biomarker. Serum BTP, with superior sensitivity and specificity, appears to be the more powerful indicator, while urinary BTP provides a convenient non-invasive alternative.

Serum and urinary Beta-trace protein exhibit outstanding diagnostic accuracy for hypertension-related renal dysfunction. The findings align with previous evidence [14,18, 20] and emphasize BTP's potential as a reliable, sensitive biomarker for early detection, staging, and monitoring of renal impairment in essential hypertension. Its close association with both renal and cardiovascular injury suggests a valuable role in comprehensive vascular risk assessment.

Strength and limitations of the study:

This study's strength lies in its comprehensive evaluation of both serum and urinary beta-trace protein (BTP) as potential early markers of renal dysfunction in essential hypertension, using well-defined patient groups and standardized ELISA measurements. However, its relatively small sample size, single-center design, and cross-sectional nature limit the generalizability and ability to assess causality. Larger multicenter longitudinal studies are recommended to validate these findings and confirm the prognostic value of BTP.

CONCLUSION

This study demonstrated that serum and urinary beta-trace protein (BTP) levels increased significantly with the severity of renal impairment in patients with essential hypertension. Both markers correlated negatively with estimated glomerular filtration rate (eGFR) and positively with serum creatinine and urinary albumin-to-creatinine ratio, indicating their strong association with renal dysfunction. Receiver operating characteristic analysis confirmed the high diagnostic accuracy of BTP, with serum BTP showing 95.8% sensitivity and specificity and urinary BTP achieving similarly high performance. Compared with conventional markers, BTP demonstrated superior sensitivity for early detection of renal injury. In conclusion, BTP serves as a valuable, non-invasive biomarker for identifying early renal dysfunction in essential hypertension and may complement traditional renal function tests. Further large-scale studies are needed to validate their prognostic and clinical utility.

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REFERENCES

1. **Johansen KL, Gilbertson DT, Li S (2024):** US renal data system 2023 annual data report: epidemiology of kidney disease in the United States. Am J Kidney Dis., 83(4):A8-13.
2. **Levey A, Coresh J, Balk E *et al.* (2003):** National Kidney Foundation practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. Ann Intern Med., 139 (2): 137-147.
3. **Stevens K, Aiyegbusi O, McGregor E *et al.* (2022):** Immunosuppression therapy in kidney transplantation. Urol Clin North Am., 49 (2): 345-360.
4. **Uehara Y (2004):** PGD(2)/L-PGDS system in hypertension and renal injury. Nihon Yakurigaku Zasshi, 123 (1): 23-33.
5. **Eguchi T, Miyauchi S (2015):** A case of primary aldosteronism with secondary hyperparathyroidism and bilateral adrenal tumors. Endocrinol Diabetes Metab Case Rep., 2015 :1.
6. **James M, Grams M, Woodward M *et al.* (2015):** A meta-analysis of the association of estimated GFR, albuminuria, diabetes mellitus, and hypertension with acute kidney injury. Am J Kidney Dis., 66 (4): 602-612.
7. **Izzo J, Black H (1993):** Hypertension Primer: The Essentials of High Blood Pressure. Dallas: Am Heart Assoc., Lippincott; 1st ed.
8. **Levey A, Bosch J, Lewis J *et al.* (1999):** A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Ann Intern Med., 130 (6): 461-470.
9. **O'Brien A, Teel L, Steinberg B *et al.* (2003):** Shiga toxin-producing Escherichia coli-associated kidney failure in a 40-year-old patient and late diagnosis by novel bacteriologic and toxin detection methods. J Clin Microbiol., 41 (7): 3438-3440.
10. **Weber C, Duchateau-Nguyen G, Solier C *et al.* (2014):** Cardiovascular risk markers associated with

arterial calcification in patients with chronic kidney disease Stages 3 and 4. Clin Kidney J., 7 (2): 167-173.

11. **Süleymanlar G, Utaş C, Arinsoy T *et al.* (2011):** A population-based survey of Chronic REnal Disease In Turkey—the CREDIT study. Nephrol Dial Transplant., 26: 1862-1871.
12. **Herget-Rosenthal S, Bökenkamp A, Hofmann W (2007):** How to estimate GFR-serum creatinine, serum cystatin C or equations? Clin Biochem., 40 (3-4): 153-161.
13. **Ma Y, Tahaei S, Couasnay G *et al.* (2018):** The reduced osteogenic potential of Nf1-deficient osteoprogenitors is EGFR-independent. Bone, 106: 103-111.
14. **Donadio C, Bozzoli L (2016):** Urinary β-trace protein: A unique biomarker to screen early glomerular filtration rate impairment. Medicine (Baltimore), 95(49):e5553.
15. **Astor B, Shafi T , Hoogeveen R *et al.* (2012):** Novel markers of kidney function as predictors of ESRD, cardiovascular disease, and mortality in the general population. Am J Kidney Dis., 59: 653-662.
16. **Hati T, Nanda B, Sahu P (2025):** Serum Creatinine and Urine Microalbumin Levels in Patients with Essential Hypertension. Int J Pharm Clin Res., 17 (1): 266-269.
17. **Huang M, Matsushita K, Sang Y *et al.* (2015):** Association of kidney function and albuminuria with prevalent and incident hypertension: the Atherosclerosis Risk in Communities (ARIC) study. Am J Kidney Dis., 65: 58-66.
18. **Hoffmann A, Nimtz M, Conradt H (1997):** Molecular characterization of β-trace protein in human serum and urine: a potential diagnostic marker for renal diseases. Glycobiology, 7 (4): 499-506.
19. **Melegos D, Grass L, Pierratos A *et al.* (1999):** Highly elevated levels of prostaglandin D synthase in the serum of patients with renal failure. Urology, 53 (1): 32-37.
20. **Dajak M *et al.* (2010):** Urinary beta-trace protein as a tubular marker of renal dysfunction in patients with chronic kidney disease. Clin Chim Acta, 411: 1154-1155.
21. **Pöge U, Gerhardta T, Palmedo H *et al.* (2005):** MDRD equations for estimation of GFR in renal transplant recipients. Am J Transplant., 5 (6): 1306-1311.
22. **Hirawa N, Uehara Y, Yamakado M *et al.* (2002):** Lipocalin-type prostaglandin D synthase in essential hypertension. Hypertension, 39: 449-454.
23. **Song W, Ricciotti E, Liang X *et al.* (2018):** Lipocalin-like prostaglandin D synthase but not hemopoietic prostaglandin D synthase deletion causes hypertension and accelerates thrombogenesis in mice. J Pharmacol Exp Ther., 367: 425-432.
24. **Elebidi A, Mai A, Abulfadl M *et al.* (2022):** Beta trace protein as a predictive biomarker of chronic kidney disease. Aswan University Medical Journal, 2(1):20-25.
25. **Grams M, Sang Y, Ballew S *et al.* (2015):** A meta-analysis of the association of estimated GFR, albuminuria, age, race, and sex with acute kidney injury. Am J Kidney Dis., 66 (4): 591-601.
26. **Nakayama H, Echizen H, Gomi T *et al.* (2009):** Urinary lipocalin-type prostaglandin D synthase: a potential marker for early gentamicin-induced renal damage? Ther Drug Monit., 31: 126-130.
27. **Vynckier L, Floré K, Delanghe S *et al.* (2009):** Urinary beta-trace protein as a new renal tubular marker. Clin Chem., 55: 1241-1243.
28. **Hebah H, Afifi E, Abd El-Megeid S *et al.* (2018):** Beta-trace protein as an early predictor of diabetic nephropathy in type II diabetes. J Egypt Soc Nephrol Transplant., 18 (3): 96-102.