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ANALYSIS OF SERUM LEVELS OF TRADITIONAL RENAL BIOMARKERS FOR THE EARLY DETECTION OF NEPHROPATHY

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Abstract:

Introduction: *Characteristic features of chronic kidney disease (CKD) involve progressive destruction of the renal parenchyma and the loss of functional nephrons. The loss of functional nephrons triggers molecular and cellular events responsible for compensatory growth of the remaining ones.* ***Aims and objectives:*** *The main objective of the study is to analyze the serum levels of traditional renal biomarkers for the early detection of pre-hypertensive nephropathy.*

Methodology of the study: *This cross sectional study was conducted at THQ Hospital, Daska during September 2018 to January 2018. Those with slightly raised serum creatinine and those with blood sugar levels within pre-diabetes range on previous reports were excluded, and so were those who gave history of antihypertensive medication or use of steroid. Informed consent was taken from all study participants.*

Results: *Of the 90 individuals initially enrolled, 12(13.3%) were excluded, leaving the study sample to be 78(86.6%). Of them, 39(50%) were normotensive in group 1 and (50%) in pre-hypertensive group 2. There were 33(84.6%) males and 6 (15.4%) females in group 1, and 36(92.3%) males and 3(7.7%) females in group 2. Serum Cystatin-C levels were 0.91 mg/l in group 1 and 1.55 mg/l in group 2 (p=0.0001) whereas serum creatinine difference in both groups remained statistically non-significant (p=0.977).*

Conclusion: *It is concluded that diagnostic markers which reflect renal impairment at early stage is important as early intervention can slow the loss of kidney function and reduce adverse clinical outcomes. Serum cystatin C rise faster than SCr after a fall in GFR and has the potential to accurately detect earlier changes in GFR compared to SCr, serving as an excellent endogenous marker of early renal dysfunction in type 2 diabetes.*

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INTRODUCTION:

Characteristic features of chronic kidney disease (CKD) involve progressive destruction of the renal parenchyma and the loss of functional nephrons. The loss of functional nephrons triggers molecular and cellular events responsible for compensatory growth of the remaining ones. These mechanisms may become pathological and result in the development of renal lesions and lead to end-stage renal disease (ESRD) [1]. The development of chronic kidney disease involves the separation of podocytes from basal membrane and their loss with urine, therefore the determination of the presence of some structural proteins connected with glomerular barrier may be helpful in the diagnosis of renal diseases [2].

The loss of function in the course of chronic kidney disease is also associated with interstitial fibrosis and inflammation. Early diagnosis of this disease is important step in the prevention of CKD complications [3]. Moreover, it is needed for the hampering of the progression to kidney failure and preventing the occurrence of cardiovascular events [4]. In clinical practice, GFR is generally estimated based on measurement of endogenous blood substances, and serum creatinine (SCr) level is the most commonly used marker for estimating GFR and assessing renal impairment [5]. However, SCr does not depend solely on GFR, and its concentration is affected by non-renal factors including age, gender, race, muscle mass, medication use, and dietary meat intake. SCr is not reabsorbed by the renal tubules, but it is secreted. The substantial tubular excretion of creatinine and the well-known sensitivity of the analytical methods, especially the Jaffe´ method, to interfering substances in the plasma (e.g., acetic acid, acetone, pyruvate, glucose, ascorbic acid, and bilirubin) are other factors that reduce the clinical utility of SCr as a marker of GFR estimate [6]. Although, the measurement of creatinine clearance overcomes some of limitations of SCr, it requires a timed urine collection, which has proven to be inconvenient and prone to collection errors [7].

Aims and objectives

The main objective of the study is to analyze the serum levels of traditional renal biomarkers for the early detection of pre-hypertensive nephropathy.

METHODOLOGY OF THE STUDY

This cross sectional study was conducted at THQ Hospital, Daska during September 2018 to January 2018. Those with slightly raised serum creatinine and those with blood sugar levels within pre-diabetes range on previous reports were excluded, and so were those who gave history of antihypertensive medication or use of steroid. Informed consent was taken from all study participants. Five millilitres of blood was collected from antecubital vein of each subject under aseptic conditions and serum was subsequently obtained through ultracentrifugation which was subsequently stored at-80 degrees Celsius in Eppendorf tubes for the measurement of biochemical parameters i.e.; Cystatin-C and creatinine. CysC is a small molecule cysteine proteinase inhibitor synthesized by all nucleated cells and filtered freely by the glomerulus. After filtration it is not secreted nor reabsorbed by the tubules, but catabolized completely and thus reflects true GFR when measured in blood. Preclinically, CysC appears to be the most sensitive marker for early proximal tubular damage in animals, although a consistent dose response relation is lacking.

Statistical analysis

Student's t-test was performed to evaluate the differences in roughness between groups. Two-way ANOVA was performed to study the contributions. A chi-square test was used to examine the difference in the distribution of the fracture modes (SPSS 19.0 for Windows, SPSS Inc., USA).

RESULTS:

Of the 90 individuals initially enrolled, 12(13.3%) were excluded, leaving the study sample to be 78(86.6%). Of them, 39(50%) were normotensive in group 1 and 39(50%) in pre-hypertensive group 2. There were 33(84.6%) males and 6 (15.4%) females in group 1, and 36(92.3%) males and 3(7.7%) females in group 2. Serum Cystatin-C levels were 0.91 mg/l in group 1 and 1.55 mg/l in group 2 (p=0.0001) whereas serum creatinine difference in both groups remained statistically non-significant (p=0.977). Mean estimated GFR (eGFR) Cystatin-10.86 ml/min in 7.85 ml/min in group 2 (p=0.0001) whereas eGFR Cockcroft-Gault (CG) equation failed to exhibit any significant statistical difference between the groups (p=0.106) (Table 1).

Table 01: analysis of comparison of Serum Cystain-C and creatinin levels

Variables	Normotensives Group=1 (n=39)	Prehypertensives Group=2 (n=39)	p-value
Serum Cystatin-C (mg/l)	*0.91 (0.818-0.964)	*1.55 (1.47-1.73)	0.0001
Serum Creatinine (mg/dl)	0.916 ± 0.163	0.917 ± 0.161	0.977
Cystatin-C-based HoekGFR (eGFRCystatin-C)ml/min	*84.17 ± 10.86	*47.40 ± 7.85	0.0001
Creatinine based Cockcroft-GaultGFR (eGFRCG)ml/min	112.3± 24.8	117 ± 23.2	0.106

DISCUSSION:

Early diagnosis of CKD and identification of those likely to progress to end-stage renal disease (ESRD) has become highly important. Existing measures including creatinine level, estimated glomerular filtration rate (eGFR) and proteinuria seem to be insufficient. Therefore, new validated biomarkers are required for CKD progression and cardiovascular disease (CVD) risk [8]. Complicated patho mechanisms of CKD development and progression require not a single marker but their combination in order to mirror all types of alterations occurring in the course of this disease [9]. On the basis of aforementioned studies, it can be concluded that a panel of biomarkers rather a single marker is required to diagnose CKD with high sensitivity and specificity and to identify persons at high risk of progression. Moreover, it seems that in not so distant future, conventional markers may be exchanged for new ones, however, the confirmation of their efficacy, sensitivity and specificity as well as the reduction in analysis costs is required [10]. The increasing number of studies concerning the search for new, sensitive and selective biomarkers useful for the diagnosis and quantitative assessment of mechanisms occurring in diseased kidneys confirms the importance of this issue [11].

More recently, *Pavkov et al*. compared values of baseline serum cystatin C, SCr, and measured GFR (mGFR) for predicting ESRD in patients with type 2 diabetes and elevated albuminuria. They found that serum cystatin C was a better predictor of ESRD than mGFR or SCr, and the predictive ability of serum cystatin C remained superior to the other filtration markers in subjects with normal or high-normal GFR, suggesting that cystatin C may allow earlier stratification of patients at high risk for progression to kidney failure. *Pavkov et al*. also suggested that the predictive value of serum cystatin C for ESRD in patients with type 2 diabetes may be enhanced beyond the gold-standard measurement of GFR because of additional renal and non-renal information cystatin C may impart [12]. Another recent study by *Liu et al*. showed that the prevalence of coronary artery disease (CAD), cerebral infarction (CI) and lower limb ischemia (LLI) caused by peripheral arterial disease (PAD) increased with cystatin C, especially the prevalence of LLI. From this, *Liu et al*. concluded that apart from renal function the detection of cystatin C concentration is of great value for screening out the patients with the angiostenosis risk of lower limb to prevent foot ulceration and amputation [13].

CONCLUSION:

It is concluded that diagnostic markers which reflect renal impairment at early stage is important as early intervention can slow the loss of kidney function and reduce adverse clinical outcomes. Serum cystatin C rise faster than SCr after a fall in GFR and has the potential to accurately detect earlier changes in GFR compared to SCr, serving as an excellent endogenous marker of early renal dysfunction in type 2 diabetes. Its levels in serum or urine might be also elevated in diabetic patients even before the appearance of microalbuminuria, and can be used as useful marker for detecting nephropathy in patients with normoalbuminuria (early nephropathy), which will allow early intervention and management of type 2 diabetic patients with DN.

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