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ANALYSIS OF SERUM LEVEL OF CYSTATIN C FOR THE EARLY DETECTION OF PRE-HYPERTENSIVE NEPHROPATHY

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Abstract:

Introduction: *Chronic kidney disease (CKD) is a common and serious complication of diabetes associated with increased risk of mortality (both all-cause and cardiovascular), progression to kidney failure, cardiovascular disease (CVD) and hospitalizations. Cystatin C (CyC) is a 13-kDa, nonglycosylated basic protein, produced at a constant rate by all nucleated cells. It is freely filtered by glomeruli and catabolized in tubules.* ***Aims and objectives:*** *The main objective of the study is to analyze the serum level of cystatin C for the early detection of pre hypertensive nephropathy.* ***Material and methods:*** *This descriptive study was conducted in District Head Quarters Hospital Rawalpindi during October 2018 till December 2018. This study was done with the permission of ethical committee of hospital. The data was collected through non-probability random sampling technique method. There were total 100 patients of age range 18 to 50 years suffering from CKD. The demographic data were collected from all selected patients. 5ml 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.* ***Results:*** *The data was collected from 100 patients of both genders. The mean age range was 45±5.67 years. The median age, blood pressure, blood urea nitrogen, serum creatinine and urine specific gravity were similar in both groups. However, patients with CKD had significantly lower hemoglobin, and higher reticulocyte counts, CRP and indirect bilirubin than those with other forms of cell disease, showing the higher hemolysis, anemia, and inflammation present in patients with CKD.* ***Conclusion:*** *It is concluded that cystatin C is the leading biomarker in the early detection of pre hypertensive nephropathy. 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.*

Key words: *CKD, hypertensive, patients, inflammation*

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INTRODUCTION:

Chronic kidney disease (CKD) is a common and serious complication of diabetes associated with increased risk of mortality (both all-cause and cardiovascular), progression to kidney failure, cardiovascular disease (CVD) and hospitalizations. Accurate estimation of glomerular filtration rate (GFR), which is usually accepted as the best overall index of kidney function, is essential for the diagnosis, staging and management of CKD [1]. GFR cannot be measured directly in humans. The "gold standard" for determining GFR is to measure the clearance of an exogenous substance, such as inulin, 51Cr-EDTA, iohexol, 125I-iothalamate and 99mTc di-ethylelene triamine penta acetic acid (99cTc-DTPA) that are exclusively excreted via glomerular filtration. However, these techniques are time-consuming, labor-intensive, expensive, and require administration of substances, so that cannot be generally applied for routine prac- tice [2]. Therefore, the measurement of an endogenous blood substance that is cleared by the kidney is used to estimate GFR [3].

Acute kidney injury (AKI) is a common complication of critical illness and carries high mortality despite significant advances in medical care. This apparent lack of improvement may result from the use of more aggressive medical and surgical interventions in an ever-ageing population [4]. On the other hand, potentially effective therapeutic interventions for AKI may currently fail because they are applied late in the course of injury after an obvious increase of serum creatinine (sCr) is observed [5]. Due to the delayed rise in sCr following injury, recent efforts have focused on identification of an early and reliable biomarker of kidney injury.

Cystatin C (CyC) is a 13-kDa, nonglycosylated basic protein, produced at a constant rate by all nucleated cells. It is freely filtered by glomeruli and catabolized in tubules [6]. In high-risk patients, serum CyC (sCyC) detected AKI 1–2 days earlier than sCr. Moreover, although CyC is normally not detected in urine, it has been found in urine of patients with tubular disease, suggesting that it is a tubular marker [7]. One drawback of use of CyC at present is a lack of recognition of its potential value for use in the general critical care setting, in which the population is heterogeneous and AKI etiology and timing are often unclear [8].

Aims and objectives

The main objective of the study is to analyze the serum level of cystatin C for the early detection of pre hypertensive nephropathy.

MATERIAL AND METHODS:

This descriptive study was conducted in District Head Quarters Hospital Rawalpindi during August 2018 till December 2018. This study was done with the permission of ethical committee of hospital. The data was collected through non-probability random sampling technique method. There were total 100 patients of age range 18 to 50 years suffering from CKD.

Exclusion criteria

Those patients who were suffering from high blood sugar levels were excluded from this study.

Data collection

The demographic data were collected from all selected patients. 5ml 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. The subjects were divided into normotensive group 1 and pre-hypertensive group 2 after blood pressure of each subject was recorded. BMI of all patients were also measured. Serum creatinine was measured by Jaffe's reaction with ready-to-use assay kit (Pioneer Diagnostics, New York, USA). GFR was estimated by standardized formulae using serum creatinine-based equation.

Statistical analysis

Statistical analysis (one way-Anova Test and Post Hoc) was performed using the SPSS software program (18.0). All results were expressed as the mean ± standard deviation (SD). As P value <0.08 was considered to be statistically significant.

RESULTS:

The data was collected from 100 patients of both genders. The mean age range was 45±5.67 years. The median age, blood pressure, blood urea nitrogen, serum creatinine and urine specific gravity were similar in both groups. However, patients with CKD had significantly lower hemoglobin, and higher reticulocyte counts, CRP and indirect bilirubin than those with other forms of cell disease, showing the higher hemolysis, anemia, and inflammation present in patients with CKD.

Table 01: Characteristics of Selected Patients

Parameter	Mean ± SEM	Range/%
Gender (Male:Female)	40:60	–
On Hydroxyurea (HU)	49	54%
Hemoglobin (g/dL)	9.2 ± 0.12	7.0–13
Reticulocyte %	9.2 ± 0.57	2.4–24.7
C-reactive protein (mg/L)	2.4 ± 0.73	0.3–28.4
Blood pressure (Systolic)	113 ± 1.4	96–157
Blood pressure (Diastolic)	63.6 ± 0.92	46–96
Urine albumin (mg/g creatinine)	132.4 ± 60.3	3.1–5145
Urine Sp. gravity	1.011 ± 0.0003	1.0–1.03
Blood urea nitrogen (mg/dL)	9.4 ± 0.57	4–36
Serum creatinine (mg/dL)	0.57 ± 0.03	0.3–1.4
Urine creatinine (mg/dL)	0.57 ± 0.03	0.19–2.33
Indirect bilirubin (µmol/L)	2.7 ± 0.26	0.7–10.4

Serum Cystatin-C levels were 0.92 mg/l in group 1 and 1.56 mg/l in group 2 (p=0.0001) whereas serum creatinine difference in both groups remained statistically non-significant (p=0.1). Mean estimated GFR (eGFR) Cystatin-C was 84.23 and 43.56 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 02: Serum cysteine levels in selected patients

Variables	Normotensive	Pre-hypertensives	P-value
Serum-Cystatin C (mg/l)	0.92	1.56	0.0001
Serum Creatinine (mg/dl)	0.92	0.54±0.156	0.1
GFR (Cystatin C) (ml/mim)	84.23	43.56±5.67	0.0001

DISCUSSION:

The pre-hypertensive Pakistani population has been documented to have higher circulating levels of various stress hormones like cortisol and aldosterone. Higher circulating levels of stress hormones have been attributable to stressful life at a younger age which will ultimately develop into full-blown hypertension and its associated complications like renal dysfunction [9]. The earlier stages of reversible kidney disease have been coined as pre-chronic kidney disease that manifests itself with the excretion of low amount of albumin protein in the urine known as microalbuminuria [10]. Hypertension leads to pathophysiological process of hyperfiltration through renal glomeruli. In our study, all normotensive and pre-hypertensive participants had undetectable protein in their urine samples [11]. However, few studies showed protein levels in the urine gradually increased with rising values of BP from pre-hypertension stage 1 to stage 2 (p<0.001). Serum creatinine was essentially measured in all participants in our study because the current method of establishment of prevalence of the renal disease has been virtually based on serum creatinine cutoff values [12].

Recently, several cystatin C-based equations have been developed for estimating GFR, and has been recommend to be used as a confirmatory test for the diagnosis of CKD in patients with mild to moderate decreased GFR as estimated from creatinine (eGFR 45-59 ml/min/1.73 m^2) and no other markers of kidney damage (e.g. ACR <30 mg/g). A recent study also suggest that cystatin C-based estimated GFR (eGFRcys) can be a useful confirmatory marker in those with creatinine-eGFR (eGFRcr) < 60 ml/min/1.73 m^2 and whose ACR is <30 mg/g. Since cystatin C is less affected by non-GFR factors, GFR estimates based on serum cystatin C may have advantages over the creatininebased estimates in diabetics [13]. In light of this, a few studies have compared the performance of cystatin C- and creatinine-based equations in diabetic patients. *Rigalleau et al*. suggest that the addition of cystatin C measurements to creatinine measurements in assessment of renal function significantly improves the diagnosis and stratification of CKD, and the estimation of GFR in diabetes [14].

CONCLUSION:

It is concluded that cystatin C is the leading biomarker in the early detection of pre hypertensive nephropathy. 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.

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