Nail Creatinine Measurement in Evaluation of Chronicity of Renal Failure

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ABSTRACT

Introduction: Renal failure is common indication for hospitalisation. Prognosis and management of renal failure depends on whether renal failure is acute or chronic especially when deciding need for permanent renal replacement treatment . So present study was done with the objectives to measure nail creatinine in CKD patients, to measure nail creatinine in AKI patients, to measure nail creatinine in normal subjects and to compare nail creatinine in AKI,CKD and normal subjects and assess utility in differentiating AKI and CKD.

Material and Methods: 3 groups of subjects were selected after history physical examination and investigations. One group includes CKD patients, other AKI patients and third one with no renal co morbidities. Finger nail clippings are collected, stored and pulverized and aqueous extract is analyzed for creatinine using Jaffes reaction

Results: 150 patients were included in the study . 50 patients each in CKD group, ARF group and normal renal functions were included. Mean nail creatiinine (mg/100g nail) in control group was 29.92, in ARF patients 30.03, and in CKD patients was 59.40. Correlation with nail creatinine for other parameters of chronicity were correlated with low hemoglobin , low calcium, raised serum creatinine ,raised phosphate and uric acid and it was significant with p value of 0.01 . 48% of CKD patients had small kidney compared to AKI and normal subjects. Creatinine had significant strong positive correlation with serum creatinine ,phosphate and uric acid levels .Nail creatinine had significant strong negative correlation with hemoglobin and calcium.

Conclusion: Nail creatinine is a cheap and noninvasive test which can be used to assess the chronicity of renal failure .

Keywords : CKD (Chronic Kidney Disease), ARF (Acute Renal Failure), Acute Kidney Injury (AKI), Serum Creatinine, Nail Creatinine, Nail Creatinine, Hemoglobin, Calcium, Uric Acid, Phosphate, Ultrasonogram

INTRODUCTION

Chronic kidney disease (CKD) is a spectrum of different pathophysiologic processes with abnormal functioning of kidney and progressive decrease in GFR(glomerular filteration rate) CKD is stratified into stages depending on GFR and albuminuria in order to predict the risk of progression of CKD [1,2,4] . CKD is irreversible and need renal replacement therapy (RRT) . Early stages of CKD is often asymptomatic.[1,4,5] According to Indian Society of Nephrology (ISN) patient presented to nephrologist at stage 5 in 47.5% for the first time when they cannot be offered anything more than renal replacement therapy.[3,6]

Acute kidney injury (AKI) is characterised by sudden impairment of kidney function resulting in retention of nitrogenous and other wastes normally cleared by kidneys and dysregulation of fluid electrolytes and acid base homeostasis[1,2] . These patients usually have worse outcome than their non AKI counterparts such as prolonged hospital stay, need for RRT, development of CKD and increased mortality. 3-7% of hospitalized patient and 25-30% in ICU patient develop AKI with 5-6% of icu admission needing renal replacement therapy .The kidneys may recover even after dialysis requiring AKI. Up to 10% among them may develop end stage renal disease [1] .

Its often difficult to differentiate between ARF from CRF when patient presents with advanced uremia for first time. There are novel biomarkers (NGAL,KIM-2,IL-18 etc available nowadays which are expensive. Some investigators proposed nail creatinine assesment can be used as a marker for chronicity of kidney dysfunction as CKD patients has higher concentrations when compared to AKI patients [7,8,9,10] . Finger nails grow at a rate of 3-3.5mm/month and toe nail grows at a rate of 1-1.5 mm/month. Nail creatinine concentration can be estimated and it reflects blood creatinine concentration at the time nail was formed[11,12] . So analysis of creatinine concentration of free edge of nail will give idea about blood concentration 4- 6 months earlier . A noninvasive and less expensive investigation as nail creatinine estimation can assess and differentiate CKD from AKI , It will be affordable and can be used in low socioeconomic set ups. An early diagnosis of CKD can help in planning further treatment options.

MATERIAL AND METHODS

Source of data

Observation study of Primary Source of Information on nail clippings of CKD, AKI and patients with normal kidney function attending medicine and nephrology department of tertiary care teaching hospital, Mysuru, during December 2015 to December 2016. Secondary source of information is from published articles, journals, books .

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Inclusion criteria

Adult subjects who have given informed consent at medicine department and nephrology department of MMC & RI and as being diagnosed to have Chronic kidney disease, Acute kidney injury and adults patients with no renal co morbidities .

Exclusion criteria

Those with diabetes, hypertension for controls, Subjects with renal disease with normal creatinine , Subjects with onycholysis and subjects with nail biting habit .

Method of collection

Three groups of subjects were selected after history, physical examination and investigations. One group includes CKD patients, other AKI patients and third one with no renal co morbidities. Finger nail clippings are collected, stored and pulverized and aqueous extract is analyzed for creatinine using Jaffes reaction .

STATISTICAL ANALYSIS

Sample size: 150, calculated using the formula n=4PQ/d2 , where P is prevalence.

Q is 1-P and d=10%=0.01(margin of error) with proportion, p1=0.579 & p2=0.421 a=5%,absolute allowable error 15%the total sample size is 86 & is rounded up to 100. Each cell sample size is 50. Statistical methods applied is descriptive statistics. Descriptive statistics included frequency, percent, mean and standard deviation. Cramer's V was employed in the present study. The One-Way ANOVA procedure produces a one-way analysis of variance for a quantitative dependent variable by a single factor (independent) variable. Analysis of variance is used to test the hypothesis that several means are equal. This technique is an extension of the two-sample t test. The Correlations procedure computes Pearson's correlation coefficient with its significance level. All the statistical methods were carried out through the SPSS for Windows (version 16.0).

RESULTS

The following were the results of the present study about nail creatinine in assessing chronicity of renal failure . Among the 150 subjects chosen for the study, 106 were male and 44 were female with a male to female ratio of 2.3:1. Mean age of total subjects was 41 years . Mean age of CKD was 50 and that of AKI was 40. Majority of AKI patients were male of 26-35 years old. Majority of CKD patients were males of 36-45 years old.

Majority of the subjects who developed AKI were secondary to sepsis (26%) followed by cardiorenal causes (18%). Among sepsis patients the primary source of infection was UTI (urinary tract infection) . Among cardiorenal patients majority was due to cardiogenic shock.

Mean serum creatinine among normal subjects was 0.76mg/dl , while that of AKI was 2.26mg/dl and CKD was 8.96mg/dl.

Mean nail creatinine in normal subjects were 29.9 mg/100g, while that of AKI was 30.03 mg/100g and CKD was 59.40mg/100g. Mean hemoglobin in normal subjects was

14.09g/dl ,while that of AKI was 13.1g/dl and CKD was 8.89g/dl (Figure-1) .

Mean calcium in normal subjects was 9.8mg/dl ,while that of AKI was 9.7mg/dl and CKD was 8.6mg/dl . Mean serum phosphate level was 3.6 meq/l in normal subjects ,while in AKI was 3.85 meq/dl and in CKD was 4.8meq/dl . Mean serum uric acid level was 6.8 mg/dl in normal subjects , while in AKI was 7.1 mg/dl and in CKD was 9.76mg/dl .

Majority of CKD patients (48%) had small contracted kidney (<7.5cm) and 16% had large kidney (>12cm).

Nail creatinine and serum creatinine had statistically significant (p value< 0.05) strong positive correlation . Nail creatinine had significant strong positive correlation with serum creatinine, phosphate and uric acid levels. Nail creatinine had significant strong negative correlation with

Parameters	Pearson coefficient	p value
Serum creatinine	0.970	0.01
Hemoglobin	0.794	0.01
Calcium	0.643	0.01
Phosphate	0.718	0.01
Uric acid	0.806	0.01

Table-1: Correlation between nail creatinine and serum creatinine, hemoglobin,calcium,phosphate and uric acid

Name of study	Normal	AKI	CKD
Present study	29.9	30.03	59.40
Jessy etal	30.1	30.9	69.2
Sud etal	35.8	36.6	93.7
Li J etal	62	69	130

Table-2: Mean nail creatinine among various studies
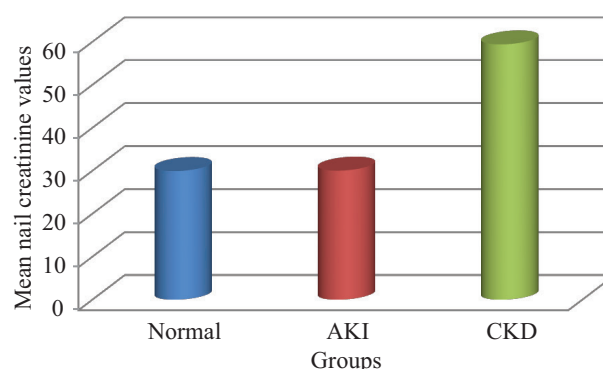
Figure-1: Mean nail creatinine in various groups

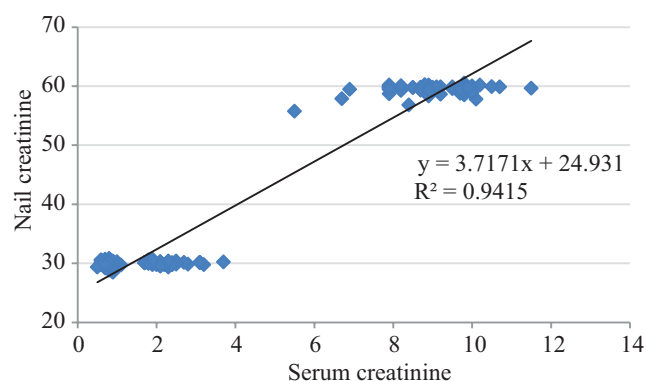
$$y = 3.7171x + 24.931$$
$$R^2 = 0.9415$$

Figure-2: Correlation between nail creatinine and serum creatinine

hemoglobin and calcium (table-2, Figure-2).

DISCUSSION

Patient presenting with advanced uremia for the first time, its often difficult to differentiate whether its an acute renal failure or acute on chronic renal failure. ARF is mostly reversible and CKD patients will need renal replacement therapy. Hence diagnosing ARF from acute on CRF is really important.

Many studies reported nail creatinine from finger tip reflects serum creatinine at the time of formation. Hence nail creatinine yields previous 6 months serum creatinine level.

Creatinine

Breakdown product of creatinine phosphate in muscle, and is usually produced at a fairly constant rate by the body (depending on muscle mass).

Biological relevance

Serum creatinine (a blood measurement) is an important indicator of renal health because it is an easily measured by-product of muscle metabolism that is excreted unchanged by the kidneys.

Creatinine itself is produced[2] via a biological system involving creatine, phosphocreatine (also known as creatine phosphate), and adenosine triphosphate (ATP, the body's immediate energy supply).

Creatine is synthesized primarily in the liver from the methylation of glycocyamine (guanidino acetate, synthesized in the kidney from the amino acids arginine and glycine) by S-adenosyl methionine. It is then transported through blood to the other organs, muscle, and brain, where, through phosphorylation, it becomes the high-energy compound phosphocreatine. Creatine conversion to phosphocreatine is catalyzed by creatine kinase; spontaneous formation of creatinine occurs during the reaction. Creatinine is removed from the blood chiefly by the kidneys, primarily by glomerular filtration, but also by proximal tubular secretion. Little or no tubular reabsorption of creatinine occurs. If the filtration in the kidney is deficient, creatinine blood levels rise. Therefore, creatinine levels in blood and urine may be used to calculate the creatinine clearance (CrCl), which correlates with the glomerular filtration rate (GFR). Blood creatinine levels may also be used alone to calculate the estimated GFR (eGFR).

The GFR is clinically important because it is a measurement of renal function. However, in cases of severe renal dysfunction, the CrCl rate will overestimate the GFR because hypersecretion of creatinine by the proximal tubules will account for a larger fraction of the total creatinine cleared.[13] Ketoacids, cimetidine, and trimethoprim reduce creatinine tubular secretion and, therefore, increase the accuracy of the GFR estimate, in particular in severe renal dysfunction. (In the absence of secretion, creatinine behaves like insulin.) Each day, 1-2% of muscle creatine is converted to creatinine.[13] Men tend to have higher levels of creatinine than women because, in general, they have a greater mass of skeletal muscle.[13]

Increased dietary intake of creatine or eating a lot of protein (like meat) can increase daily creatinine excretion.[13] Serum creatinine does not increase until the GFR has moderately decreased (about 40 ml/min/1.73 m²). This insensitivity for small to moderate decreases in GFR in creatinine blind GFR area (40-70 ml/min/1.73 m²) gives a false sense of security and leads to late detection of kidney damage. All this makes serum creatinine less reliable for making therapeutic decisions in critically ill patients, such as decision to change nephrotoxic drugs or measures to increase renal perfusion.

Diagnostic use of serum creatinine and urine creatinine
Serum creatinine

Measuring serum creatinine is a simple test, and it is the most commonly used indicator of renal function.[13]

A rise in blood creatinine level is a late marker, observed only with marked damage to functioning nephrons. Therefore, this test is unsuitable for detecting early-stage kidney disease. A better estimation of kidney function is given by calculating the estimated glomerular filtration rate (eGFR). eGFR can be accurately calculated using serum creatinine concentration and some or all of the following variables: sex, age, weight, and race. The typical human reference ranges for serum creatinine are 0.5 to 1.0 mg/dL (about 45-90 μmol/L) for women and 0.7 to 1.2 mg/dL (60-110 μmol/L) for men. The significance of a single creatinine value must be interpreted in light of the patient's muscle mass. A patient with a greater muscle mass will have a higher creatinine and it indicate normal kidney function in a male body builder, while mild increase in serum creatinine indicate significant renal disease in elderly female. Creatinine levels may increase when an angiotensin inhibitor (ACEI) or angiotensin II receptor antagonist (or angiotensin receptor blocker, ARB) is taken. Using both ACEI and ARB concomitantly will increase creatinine levels to a greater degree than either of the two drugs would individually. An increase of <30% is to be expected with ACEI or ARB use

Urine creatinine

Creatinine concentration is also checked during standard urine tests. Normal creatinine levels indicate the test sample is undiluted, whereas low amounts of creatinine in the urine indicate either a manipulated test or low individual baseline creatinine levels. Test samples considered manipulated due to low creatinine are not tested, and the test is sometimes considered failed.

Nail creatinine

As serum and urine creatinine, nail creatinine can also be assessed. Levitt[9] in 1965 for the first time suggested that the concentration of fingernail creatinine could be used as a marker of the duration of azotemia.[7,8] He found that patients with CRF had higher creatinine concentrations in the finger nails as compared to controls. Bergamo et al largely confirmed the findings. Many studies confirmed the same results.[8] Studies suggested that the amount of creatinine that enters the fingernail plate during its formation is proportionate to the serum creatinine at the time of nail formation and remain unchanged till the growth of the nail,[10]

analysis of creatinine concentration of the clipped free edge of the nail which was formed many months earlier would provide a means of estimating blood creatinine which was present at that time.[7,8,9] The amount of creatinine from the clippings at the tip of nails represent the creatinine levels 4-6 months[10] earlier. If the nail creatinine is higher than normal suggest chronicity.[11,12]

In present study equal proportion of three groups were selected which is comparable to Jessy et al study. In Sud et al study 66% of subjects were CKD patients while Li J et al study included 47% normal subject. Bergamo et al study included 64.3% CKD patients in their study. In present study normal subjects were of younger age compared to AKI and CKD patients. While in Jessy et al mean age was closer in three groups and similar age group were included in the study. In present study nail creatinine was lower in normal subjects and AKI patients and was higher in CKD which was similar to other studies by Jessy et al, Sud et al and Li J et al. Mean nail creatinine in CKD was comparable in our study with Jessy et al and Sud et al while it was higher in Li J et al. Mean serum creatinine was comparable in control group with Jessy et al study. Mean creatinine was higher in AKI and CKD in Jessy et al study as compared to present study . Mean serum calcium was lower in CKD when compared to AKI and control group in present study and Jessy et al. Mean serum phosphate was higher in all groups in Jessy et al study compared to present study . Mean uric acid levels were higher in all groups in present study compared to Jessy et al study .

Limitations of the study
1. Small sample size of the study population.
2. Age matching was not proper in all groups
3. Proper standardization of procedure to be done

CONCLUSION

In advanced uremia with non-available previous records, it is often difficult to distinguish chronicity of kidney failure. So the present study was conducted to assess utility of nail creatinine in evaluation of chronicity of renal failure. Among 150 subjects chosen for the study, 106 were male and 44 were female with a male to female ratio of 2.3:1. Mean age of controls was 35 and that of CKD was 50 and AKI was 40. Majority of subjects were male of 26-35 years of age. Majority of patients who developed AKI were secondary to sepsis (26%) followed by cardiorenal syndrome (18%). 44% of CKD patients were hypertensive. Mean nail creatinine in normal subjects were 29.9 mg/100g while that of AKI was 30.03 and controls was 29.9 mg/100g of nail. Nail creatinine showed statistically significant (p value<0.05) and strong positive correlation with serum creatinine, phosphate and urate levels. Nail creatinine showed statistically significant (p value<0.05) and strong negative correlation with hemoglobin and serum calcium level. Hence nail creatinine is a cheap and noninvasive test which can be used to assess the chronicity of renal failure if procedure being properly standardized.

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