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Assessment of Sensitivity of Renal Function Tests in Diagnosis of Chronic Renal Failure

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Abstract:

Background: The symptoms of worsening kidney function are unspecific. Laboratory evaluation may be only way of detecting disease. Laboratory tests should detect abnormalities early enough for diagnosis and treatment modalities.

Aims & Objectives: To assess sensitivity of various Renal Function Tests in diagnosis of CRF.

Materials & Methods: CRF patients of age more than 20 years were included. Four RFTs
Sr. creatinine, Blood urea, Sr. uric acid and GFR were estimated.

Results & Observations: As compared to control, in CRF urea value is increased by 5.3%, creatinine by 6.9%, uric acid by 2%, GFR decreased by 14%. At a particular degree of kidney damage the deviation in Sr. uric acid is negligible. For urea, the deviation is large; but is influenced by factors like diet. The deviation in creatinine is large. However, the values are numerically small & error tolerance is small. Also age and sex are never considered in expressing Sr.creatinine. The deviation in GFR is largest; the values are numerically high and have more error tolerance. In GFR, age and sex are considered.

Conclusion: GFR is more accurate and sensitive index of kidney damage and should be the test of choice.

Key words: Chronic renal failure, Glomerular filtration rate, MDRD, CRF, GFR

Introduction:

Chronic kidney disease (CKD) is an irreversible reduction in renal function.[1-4] It is an important source of long term morbidity and mortality. The symptoms of worsening kidney function are unspecific or patients remain asymptomatic until the disease has significantly progressed. Hence, laboratory evaluation may be only way of detecting disease. In terms of Glomerular Filtration Rate (GFR), CKD is defined as kidney damage or a GFR below 60ml/min per 1.73m2 for 3 months or more.[5]

In most of the clinical biochemistry laboratories, blood urea, serum creatinine, serum uric acid are done as renal function tests. However, it is not known whether these tests are sensitive enough for early detection of impaired renal function. If they are not, then which other tests or investigation should be used.

Currently in clinical practice, serum creatinine is the most widely used method of assessing renal function.[6] However, serum creatinine levels remain within the normal range even when renal function is

significantly impaired.[7] Despite the fact that serum creatinine alone may not be well correlated with true GFR, many clinicians continue to rely solely on serum creatinine alone as a measure of renal function and they interpret a normal serum creatinine as indicating normal renal function.[8]

This present study was designed to assess the sensitivity of various renal function tests and find the most sensitive and specific amongst them for diagnosis of chronic renal failure (CRF).

Materials and Methods:

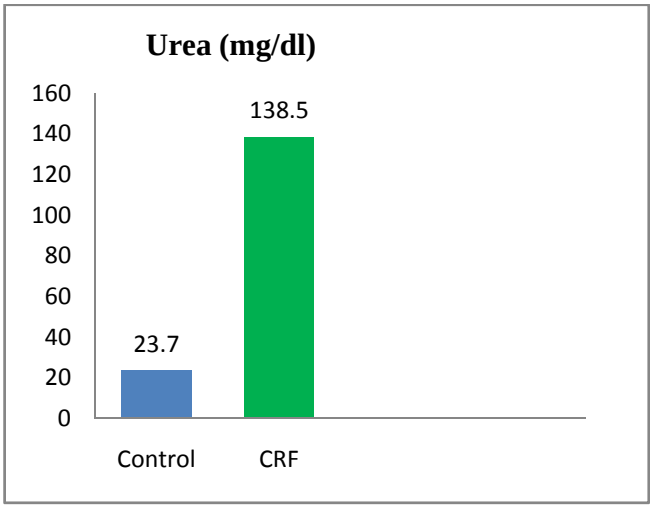
Fifty patients with age more than 20 years were included in control group and fifty patients with chronic renal failure were included in the study. Procedures were approved by the relevant local research ethics committee, and written consent was obtained from informed patients. The serum was assessed for urea, creatinine, uric acid and GFR. Serum creatinine was assessed by modified Jaffe's kinetic method.[9] Blood urea was estimated by Berthlot method.[10,11] Serum uric acid estimated by Uricase method.[12,13] GFR was estimated using modified MDRD (modification of diet for renal disease) equation.[14-18]

GFR= 175x Sr Cr-1.154 x age-0.203 x 1.212 [if black] x 0.742 [if female]

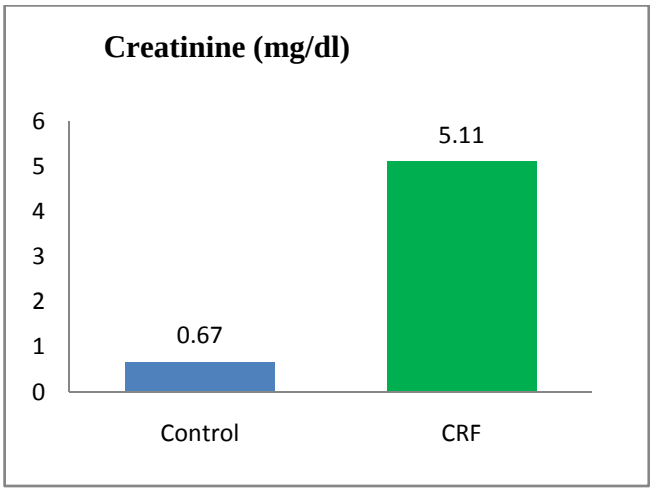
Result:

In the present study it was found that in CRF as compared to control, urea value increased by 5.8% which is highly significant. In case of creatinine, values increased by 7.63% which is also highly significant. Uric acid levels increased by 1.71% which is significant. The GFR values in CRF patients decreased by 9.11% which is highly significant. Here, when compared the degree of deviation of test values from control, GFR shows the maximum deviation.

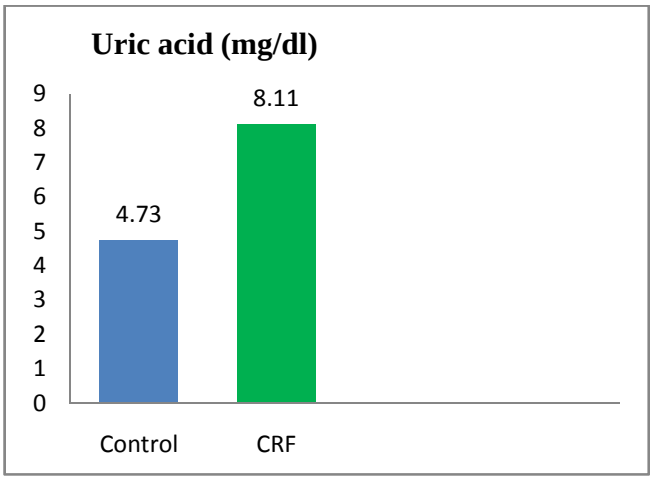
Graph 1: Comparison of urea level among control group and CRF patients



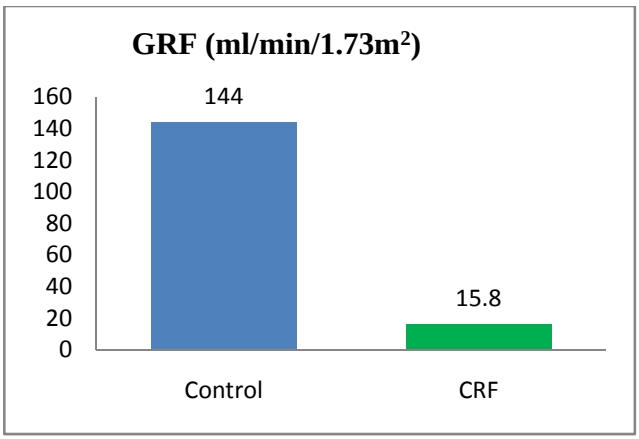
Graph 2: Comparison of creatinine level among control group and CRF patients



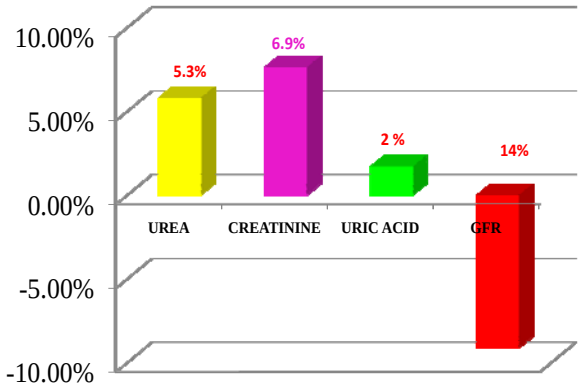
Graph 3: Comparison of uric acid level among control group and CRF patients



Graph 4: Comparison of GFR among control group and CRF patients



Graph 5: Compare the degree of deviation of test values from control, GFR shows the maximum deviation.



Discussion:

Renal function in nephrology is an indication of the state of the kidney and its role in renal physiology. Kidney's main function is excretion of nitrogenous compounds.[19] These compounds include metabolites of purines that is Uric acid and end products of protein metabolism like urea and creatinine. The renal function tests are important in assessing the excretory function of the kidneys and aids in diagnosis of chronic kidney disease and adjust the dosage of medications for renal clearance.

Urea is produced as a breakdown product of protein. It is completely filtered by the kidney but is also reabsorbed.[20] It is influenced by other factors like diet.[21,22] Thus, blood urea estimation is neither a specific nor a sensitive marker of renal function. Creatinine is a byproduct of creatine which is involved with muscle energy metabolism.[20] A relatively small amount of creatine in the body is converted to creatinine daily. This creatinine is filtered from the blood by the kidneys and excreted into urine.

Creatinine is mostly filtered by glomeruli[21] and rarely absorbed by renal tubules; therefore most creatinine is expelled from the body through urine.

In kidney disease, creatinine accumulates in the body and becomes harmful. There are two factors which affect creatinine levels, these are age and sex.[21] These two factors are never considered while expressing creatinine values. Also the control values and values in patients are numerically small; hence error tolerance in serum creatinine is small. This can give erroneous results. Also when GFR drops to one third of normal rate, the level of serum creatinine begins to rise significantly. So serum creatinine is not sensitive to even substantial decline in GFR.[6,23] Thus, serum creatinine is specific but not sensitive.

In case of uric acid, increased levels are seen due to increased synthesis or decreased excretion of uric acid. Increased synthesis is seen in Glycogen storage disease type 1, in non-vegetarian diet and in some malignancies.[24] Decreased excretion is seen in Chronic kidney disease and chronic alcoholism.[25] Thus it is neither sensitive nor specific marker.

For early diagnosis or to delay further damage a sensitive and specific marker is required. For this, in this study, Glomerular filtration rate has been estimated to evaluate its use as a sensitive and specific kidney function test. Glomerular filtration rate refers to the amount of blood that is filtered by the glomeruli per minute.[26] When kidney function declines due to damage or disease, the filtration rate

decreases and waste products begin to accumulate in the blood. The gold standard method for measurement of GFR is the clearance studies by exogenous markers such as iohexol, iothalamate, Cr51-EDTA.[27] But these procedures are costly, time consuming and they are not suited for the routine detection of kidney disease.

Hence, GFR is assessed to screen and detect early kidney disease and to monitor kidney status. There are various formulae for calculating e GFR; in this study the one recommended by National Kidney Foundation i.e. MDRD was used. This MDRD equation requires sr. creatinine, age and assigned values based upon gender and race.[16,28] Urea and uric acid are neither sensitive nor specific. Creatinine and GFR are specific but at a particular degree of kidney damage the change in creatinine values is small as compared to GFR, suggesting GFR to be more sensitive.[29] Also the values of GFR are numerically high, hence has more error tolerance. While calculating GFR, the factors affecting it like age, sex and race are considered; thus nullifying their effect. Calculating GFR is also easy and cheap. It does not require any tedious job like 24 hrs urine sample collection; it just needs serum creatinine value which is routinely done in laboratory. Also, innovative charts can be prepared for various age to calculate age-**0.203** required in MDRD equation, making the calculation part easy.

Finally, the differences in the way the kidneys handle urea, creatinine and uric acid is of diagnostic value. From earlier discussion, it is clear that urea is neither sensitive nor a specific marker. Creatinine is specific but not a sensitive marker. Uric acid is also neither sensitive nor specific marker; whereas, GFR is both sensitive and specific marker.

So, GFR can be a useful index to measure renal function in addition to the routinely used renal function tests.

Conclusion:

GFR is more accurate and sensitive index of kidney damage and should be the test of choice. It aids in early diagnosis and prevention of complications of chronic renal failure. Recommendations from this study are limited by other parameter like cystatin C which is not included in this study.

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Patient consent-Obtained

Ethics approval-Taken

Competing interests- None to declare

Contribution-

1. Kapila Gaikwad- Conception and design, acquisition of data or analysis and interpretation of data, did the laboratory investigations, did the literature search, drafted the manuscript and approved the final version.
2. Nitin Joshi did the literature search and did the final drafting of the manuscript.

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