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USE OF ANALYTE FACTORS FOR THE DIAGNOSIS OF CHRONIC RENAL FAILURE

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ABSTRACT

The factor obtained by dividing the concentration of one analyte by another are very rarely used for laboratory diagnostic purposes except the use of traditional old albumin/globulin. Recently some cardiologists make use of the factor obtained using Total Cholesterol/ HDL-C or LDL-C/HDL-C for diagnostic purposes. In other package tests such as renal profile, thyroid profile, diabetic profile, such factors are not being used and very few studies have been done in this aspect. This study presents a new concept in laboratory diagnosis of renal diseases particularly chronic renal failure by doing a host of 6 important biochemical analytes, the so called renal package tests. The first line of quantitative tests are measurements of urea and creatinine. Once the value obtained for Urea/Creatinine is >20 or more, further measurements of calcium, phosphorus, urate and magnesium will help the clinicians to confirm Chronic Renal Failure based on the values obtained between any two analytes and comparing with the normal values for such factors. It is interesting to observe from the results obtained if Urea/Creatininefactor becomes >20, all other analytes values are found to be greater than the normal values for each factor suggesting that additional tests like calcium, phosphorus, magnesium and urate will certainly help to confirm Chronic Renal Failure diagnosis. The outcome of this study will help

clinical laboratories to make use of these findings to diagnose Chronic Kidney Failure patients and extent this usage for the diagnosis of other diseases by measuring the package tests.

Keywords: Urea, Creatinine, Calcium, Phosphorus, Urate, Magnesium, Chronic Renal Failure

INTRODUCTION

The goal of treatment for chronic kidney disease is to prevent or slow further damage to the kidneys. Conditions such as diabetes or high blood pressure usually causes kidney disease and hence it is important to do laboratory tests and diagnose to manage the condition that is causing kidney disease. It is also important to prevent diseases and avoid situations that can cause kidney damage or make it worse. Several biochemical function tests are used to screen and differentiate the causes for renal disease, and to determine the extent of renal dysfunction. These tests attempt to define the clinical state of renal dysfunction and not the process of injury. A host of laboratory tests are used for the diagnosis of kidney diseases, starting from urine micro, sugar and albumin to quantitative tests like urea, creatinine, uric acid, calcium and phosphorus. Each test is individually used in comparison with the normal range, but the use of the factors obtained between two analytes have not been properly utilized. This paper aim to bring out the clinical utility of using the factor obtained between two analytes in the form of anlayte 1/analyte 2 and comparing the value with the established normal factors. The factors obtained for a selected number of kidney disease patients were then compared with the normal factors to find out the level of significance, and recommended its use for routine clinical purposes.

Severely disproportionate Blood Urea Nitrogen (BUN): Creatinine (Cr) is frequently multifactorial and is most common in the elderly, perhaps due to their lower muscle mass, and in Intensive Care Unit patients who are given a high protein intake. It is often not indicative of uncomplicated renal hypoperfusion, although low renal perfusion (hypovolemia, shock, or heart failure) is common. Mortality is high due to the severe illnesses, especially infection, worsened by decreased renal function and hypercatabolic state **[1]**.

Congestive heart failure was the most common identifiable cause of a raised plasma urea concentration in the 100 unselected patients (36%). Among these 100 patiets the plasma creatinine concentration was a more useful discriminant between pre-renal

uraemia and intrinsic renal failure than was the urea: creatinine ratio or the plasma urea concentration. A plasma creatinine concentration greater than (2-8 mg/dL) indicates intrinsic renal failure with a 90% probability **[2]**.

Black stool, age less than 50 years, and blood urea nitrogen/creatinine value of 30 or greater independently predict an upper Gastro Intestinal Tract (GIT) and bleeding source **[3]**. Measurement of BUN/Cr (BCR) is useful for localizing the source of bleeding to the upper GIT and also demonstrates its usefulness as an estimation of the severity of blood loss from the upper GIT **[4]**.

There is little evidence that BCR can distinguish between these two conditions and/or is clinically useful. Approximately half of the patients with acute kidney disease (AKI) have a BCR >20, the traditional threshold of diagnosing Pre Renal Azotemia (PRA). Unlike PRA patients who have a lower mortality than Acute Tubular Necrosis (ATN), high BCR patients had higher hospital mortality compared with low BCR patients, which was confirmed with multivariable analysis. These findings do not support BCR as a marker of PRA **[5]**.

A BCR >20 is associated with increased mortality in critically ill patients. It is also associated with a lower likelihood of Renal Replacement Therapy (RRT), perhaps because of misinterpretation of the BCR,clinicians should not use a BCR >20 to classify AKI in critically ill patients **[6]**.

MATERIALS AND METHODS

After thoroughfully going through the literature review in connection with the project topic, a reasonable number of 100 non hospitalized patients attending nephrology clinic and whose serum creatinine levels >5 mg/dL were selected for this study. This consisted of both males and female in the age group of 18 to 75 years.

As the sole aim of this study is to use the analytes urea, creatinine, uric acid, calcium, phosphorus and magnesium and as the factor obtained by dividing one analyte value by other, for diagnosis of Chronic Renal Failure (CRF) inclusion or exclusion criteria were not followed. Olympus AU400 analyser was used to measure all the analytes. Urea was measured by urease-GLDH method, Creatinine by Jaffe'smethod, Uric acid by Uricase, Calcium by Arsenazo III dye binding method, Magnesium using xylidyl blue dye binding and phosphorus by UV kinetic.

RESULTS

All the results obtained in this study have been presented in **Table 1** such as Analyte I / Analyte 2, population mean, sample mean, sample SD and critical ratios. The critical

ratios were used to find out the probability referring to Appendix V of the above mentioned reference text book on Biostatistics.

While all the analytes compared between population mean & sample means are highly significant at $p<0.0001$, only P/Mg shows a significant of <0.01. It is quite evident from these comparisons that the factors obtained in terms of analyte/analyte 2 indeed shows that all the analytes measured in this study are useful for the diagnosis of chronic renal failure.

Statistical Analysis

Critical ratios (CR) were calculated using sample mean and SD in comparison with population mean. critical ratio was calculated using formula **[7]**:

$$CR = \frac{\text{Difference in Means}}{\text{Estimate of the Standard Error of Mean}}$$

Table 1: Analyte1 / Analyte 2 Values for Normal and Patient Group (n=100), Mean, SD and Critical Ratio

S. No.	Analyte	Population (Normal) Mean	Patient (Sample) Mean	Sample SD	Critical Ratio
1.	Urea/creat	31.7	18.5	7	18.9
2.	Urea/Ua	5.3	20.7	7.9	19.5
3.	Urea/Ca	2.9	23	11.5	17.5
4.	Urea/P	7.5	24.9	11.8	14.8
5.	Urea/Mg	13.4	51.5	35.6	10.7
6.	Creat/Ua	0.17	1.2	0.5	20.6
7.	Creat/Ca	0.09	1.3	0.5	24.2
8.	Creat/P	0.25	1.4	0.6	19.2
9.	Creat/Mg	0.41	2.8	1.7	14.1
10.	Ua/Ca	0.54	1.1	0.5	4
11.	Ua/P	1.4	1.2	0.5	5.6
12.	Ua/Mg	1.65	2.6	1.7	28.3
13.	Ca/P	2.9	1.2	0.6	17.9
14.	Ca/Mg	4.9	2.4	1.4	2.5
15.	P/Mg	1.8	2.1	1.2	11.2

DISCUSSION

The first line of laboratory testing for the diagnosis of renal failure is the measurement of blood urea and creatinine and among these two analytes, creatinine is a better marker as the level is unaffected by diet rich in proteins. However, urea/creatinine value is an important indicator to further substantiate the diagnosis, the other analytes which are altered in renal failure patients are Calcium, Phosphorus, Urate and Magnesium. The values obtained between any two analytes were also found to be high compared to

normal population indices for those analytes for renal failure patients.

Very few studies have been done regarding the usefulness of such factors obtained as was done in this study. Only BUN/Creatinine has been used to assess the severity of renal dysfunction **[4]** and a value of >20 is highly suggestive of increased mortality and our findings correlate with that study **[6]**.

CONCLUSION

This study presents a new concept in laboratory diagnosis of renal diseases particularly chronic renal failure by doing a host of 6 important biochemical analytes. Once the value obtained for Urea/Creatinine is >20 or more, further measurements of Ca, P, urate and magnesium will help the clinicians to confirm CRF based on the values obtained between any two analytes. It is interesting to observe from the results obtained that if Urea/Creatinine becomes >20, all other analytes values are greater than the normal values suggesting that additional tests like Ca, P, Mg and urate will certainly help to confirm CRF cases. The outcome of this study will help clinical laboratories to make use of these findings to diagnose CRF patients. Such studies could be extended for the diagnosis of other diseases like Diabetes, Cardiac, Thyroid to name a few. Such studies could also be extended to urine based diagnostic technologies.

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