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Original Research Article

Laboratory characterization of patients with chronic renal failure in resource-limited settings, with special reference to the post-COVID-19 milieu

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ABSTRACT

Chronic kidney disease (CKD), a known global burden involving costly diagnostic and therapeutic modalities, is rampant in urban Indian localities. This study attempts to characterize a subset of proven CKD patients attending out-patient municipal clinics and dispensaries in Mumbai, with an emphasis on the post-COVID scenario. A cross-sectional and longitudinal study was executed in 60 such subjects along with an appropriate number of normal, healthy controls, who were routinely monitored i) up to March 2020, and ii) post-April 2022, the intervening period overlapping with extremely poor and even negligible patient attendance during the COVID-19 pandemic. CKD was estimated by its two most often utilized surrogate markers, serum creatinine and blood urea nitrogen. Amongst the participants, we observed slightly increased values in the aforesaid biomarkers, the underlying aetiology of which has not, to our knowledge, been studied in detail. We recommend comprehensive additional studies in order to corroborate our findings.

1. Introduction

Chronic kidney disease (CKD) or chronic renal failure (CRF), as it is variously known, is a well-defined and significant global health burden,[1] with substantial socioeconomic ramifications. It is defined as presence and persistence of any of the following: estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73 m^2, albuminuria ≥30 mg/24 hours, or markers of kidney damage (e.g. isolated proteinuria or structural abnormalities of the kidneys) for more than 3 months.[2]

The past fifty years or so, in particular, have witnessed a steady and persistent increase in its prevalence.[3] It is known to affect more than 10% of the general population worldwide, currently amounting to over 850 million individuals.[4] Misdiagnosed or left untreated, it can assume morbid proportions, and may burgeon into acute renal failure, ultimately leading to costlier and complicated therapeutic regimes, including dialysis and even transplantation as the final line of treatment. Standard diagnostic procedures are complex and expensive requiring imaging techniques and state-of-the-art renal biopsies involving histopathological and electron microscopy procedures, not always available in primary health care settings. Classical biochemical analysis involving the

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estimation of non-protein nitrogenous end products of metabolism, i.e., serum creatinine and blood urea nitrogen (BUN) is often the method of choice in resource-limited settings, such as municipal clinics and out-patient departments. The normal range of serum creatinine varies from 0.5 – 1.2 mg/dl (44 – 106 μmol/L) in adults; the corresponding figures for urea nitrogen in blood or serum is 5 – 21 mg/dl (1.8 - 7.1 mmol urea per litre),[5] all values stated being the average across both sexes.

Serum and urine creatinine levels are the most common used tests to evaluate GFR and renal functions routinely.[6,7] These are good markers of GFR because of low intra-individual variations, endogenous presence of creatinine, and full filtration from glomerular and no tubuler reabsorption. But, there are some disadvantages such as it is affected by age, sex, race, muscle mass, diet, exercise, thyroid functions, and extra-renal elimination and tubular secretion.[8] Again, twenty-four hours urine test is not recommended for GFR calculation because of urine collection errors, trouble to patients, incomplete bladder discharge and >25% of between-day variations of creatinine clearance.[9] Moreover, serum creatinine is a more accurate assessment of renal function than urea, even though urea is increased earlier in renal disease.[10] Nephrologists prefer estimated GFR (e-GFR) of serum creatinine to creatinine clearance because of the change caused by age, sex, race, and wider reference ranges of serum creatinine and limitations of 24-hours creatinine clearance test.[11]

Urea, on the other hand, historically the first marker used to formally assess kidney function, is the major form of nitrogenous waste in the body.

eventually, BUN was introduced as a routine diagnostic test in the 20th century.[12] But serum creatinine (Scr) gradually superseded BUN for the assessment of kidney function. Today, by itself, BUN is not the ideal marker to assess GFR. Combined with plasma creatinine as a creatinine/BUN ratio, however, it can be a useful analyte in differentiating pre- or post-renal increase of plasma non protein nitrogenous substances (NPNs).[13]

The World Health Organization declared the novel coronavirus (COVID-19) outbreak a global pandemic as a pandemic on March 11, 202015, and soon after, India announced its first lockdown on March 24, 2020. It was only from April 2, 2022, more than two years later, that most Covid-19 related restrictions enforced under the Epidemic Diseases Act and Disaster Management Act were withdrawn by the Government of Maharashtra. This eventuated in patients gradually revisiting OPD clinics like in pre-COVID times.

The long-term impact of COVID-19 infection on kidney function is poorly defined owing to paucity of studies and a lack of the understanding of the precise causal effects of viral infection upon renal dysfunction.[14] It is difficult to pinpoint the exact reason underlying the increased (albeit slightly) post-COVID values in serum creatinine and BUN observed in some individuals, which may lead to a poorer prognosis of the disease in this particular subset of patients. Similar associations have been reported in recent literature.[15,16]

This project attempts to study the changes, if any, in patients with chronic renal failure that may be predictable over a prolonged duration which largely coincides with the onset and the ensuing extended prevalence of the COVID-19 pandemic for roughly two years.

2. Aims and Objectives

To study the impact of COVID -19 Pandemic on the biochemical parameters in patients with chronic kidney diseaase.

To study the serum creatinine, blood urea nitrogen and BUN/Creatinine ratio in chronic kidney disease patients, in reference to pre and post COVID -19 pandemic.

3. Materials and Methods

3.1. Study design and settings

Participants for the proposed study were chosen randomly from amongst adult individuals attending out-patient departments of the municipal dispensary located in the vicinity of B.Y.L. Nair Municipal Hospital, and presenting with various symptoms of chronic renal failure and those who were undergoing treatment at B.Y.L. Nair charitable Municipal Hospital, Mumbai Central, Mumbai. A sizable number of healthy, asymptomatic controls with clinically normal values of serum creatinine and blood urea nitrogen were recruited into the study, being relatives or acquaintances of the patients, belonging to the same socioeconomic strata, and with similar dietary habits.

The study itself was cross-sectional, including individuals irrespective of class, creed, and gender, the only criteria being that they were above 18 years of age. By its very purpose and definition, the study was also longitudinal and partly retrospective, as laboratory measurements were reproduced over long duration, to facilitate segregation and comparison of key biochemical parameters in demarcated pre-COVID-19 and post-COVID-19 phases. This could also result, to a limited extent, in a better understanding of disease progression as a function of time.

Screening was done on the basis of proven chronic kidney disease, confirmed at the laboratory stage, through raised values of serum creatinine and / or blood urea nitrogen. Prior informed consent was duly received from all participants. Accordingly 60 patients were finally included in the study group, from amongst the originally identified 76 patients, eleven being lost to follow-up owing to relocation or untraceability, five having expired, out of which two had succumbed to the COVID-19 infection.

Table 1: Pre-covid characteristics

	Control (n=30)	Samples (n=60)	Mann-whitney U	Z	P
BUN	13.020	60.50	0.0000	-7.7043	0.0001
Sr.Creatinine	0.7657	2.2762	0.000	-7.72095	0.0001
BUN/Creatinine	60.60	37.95	447	-3.87742	0.0001

Table 2: Post-covid characteristics

	Control (n=30)	Samples (n=60)	Mann-whitney U	Z	P
BUN	13.617	39.082	0.0000	-7.70983	0.0001
Sr.Creatinine	0.8090	3.3273	0.0000	-7.70656	0.0001
BUN/Creatinine	63.10	36.70	372	-4.5999	0.0001

Table 3: Nonparametric WILCOXON signed rank test (Pre V/S Post value)

		Willcoxon z value	P
BUN	Controls	-.2.584	0.010
	Samples	-6.438	0.000
Sr.Creatinine	Controls	-2.661	0.008
	Samples	-0.6738	0.000
BUN/Creatinine	Controls	0.822	0.411
	Samples	-3.037	0.02

Both the core study group and normal, healthy controls have been routinely monitored i) up to March 2020 or earlier, and ii) post-April 2022, the intervening period overlapping with extremely poor and even negligible patient attendance during the COVID-19 pandemic.

3.2. Phlebotomic analysis

Venous blood was collected in a 5 ml BD Vacutainer® SSTTM tube. The serum thus separated was sufficient for estimation of both creatinine and BUN. If not processed immediately, the tubes were frozen and tested within a week's time, avoiding repeated freezing and thawing.

3.3. Laboratory analysis of key biochemical parameters

The biochemical profile tested for this particular study was confined to assessing the most routinely use markers of renal function, namely, serum creatinine and blood urea nitrogen; both being quantitatively estimated by utilizing standardized and easy-to-use kits (Pathozyme Diagnostics).

Briefly, creatinine was colorimetrically determined by the fixed time kinetic modified Jaffe's method,[17] based on the principle that creatinine forms an orange-coloured complex with picric acid in an alkaline medium. The intensity of the colour formed within a fixed time (measured at a wavelength of 505 nm) is directly proportional to the amount of creatinine present in the sample.

In contrast, BUN is quantitatively estimated by the UV-GLDH method, based on an adaptation of the enzymatic method of Talke and Schubert.[18] In this method, urea is hydrolyzed enzymatically by urease to yield ammonia and carbon dioxide. The ammonia and α-oxoglutarate are converted to glutamate in a reaction catalyzed by L-glutamate dehydrogenase (GLDH). Simultaneously, a molar equivalent of reduced NADH is oxidized. Two molecules of NADH are oxidized for each molecule of urea hydrolyzed. The rate of change in absorbance at 340 nm, due to the disappearance of NADH, is directly proportional to the BUN concentration in the sample.

4. Results

There is significant difference among mean rank of each test between Group C and S in both period Pre and Post COVID.(Tables 1 and 2)

5. Discussion

In present study, we studied pre- covid and post- covid monitoring of CKD, in this we used standard renal function markers such as BUN, sr. Creatinine, BUN/Creatinine. There is significant difference among mean rank of each test between control and sample groups, in both period PRE and POST COVID. There is deterioration of renal health, which is seen through increase in serum creatinine levels. This deterioration is statistically significant, though this study have not investigated the detailed causative factors for the deterioration. We assume this change due to possibly decreased number of follow-up visits to routine health facilities during covid pandemic. However, this is limitation of this study to investigate the causative factors for the results obtained. Our study findings are well co relating Henry B.M., Lippi G.[15] and *Extance A.*[16] Those needing long term medical care are among the groups hardest hit by coronavirus. Andy Extance asks how isolation and evolving

procedures and systems are affecting patients.[16]

6. Conclusion

The mean rank of each test significantly increases between PRE and POST COVID-19 period, this clearly indicate the lack of follow-up due to various reasons during lockdown period. Hence, we conclude, regular follow-up and assessment of laboratory parameters such as blood urea nitrogen, serum creatinine and BUN to serum creatinine ratio can be of better utility, as it can be more valuable in determining the presence as well as monitoring the progress of intrinsic (organic) or extrinsic (functional) renal disease.[19]

7. Source of Funding

None.

8. Conflict of Interest

None.

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