Original Article

Comparison of Pre and Post Anaesthetic Urinary Protein in Patients of Chronic Kidney Disease undergoing Abdominal Surgery under General Anaesthesia

Dr. Rakesh Kumar Sinha[1], Dr. Niraj Kumar Mishra*[2], Dr. Deepak Kumar[3]

1. Senior Resident, Department of Biochemistry, AIIMS, Patna, Bihar, India.
2. Senior Resident, Department of Anesthesiology and Critical Care, Darbhanga Medical College and Hospital, Lehariasarai, Bihar, India.
3. Tutor, Department of Pharmacology, Government Medical College, Bettiah, Paschim Champaran, Bihar, India.

***Corresponding author's E-mail:** mishraniraj3315@gmail.com

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ABSTRACT

Introduction: Multiple factors, including hypovolemia, low systemic vascular resistance brought on by anaesthesia or compression of inferior vena cava during surgical procedures are known to increase the risk of post-operative acute kidney injury in patients with chronic kidney disease. Novel approaches, such as the utilization of biomarkers to determine the likelihood of acute kidney injury are required to more accurately identify pre-operative renal dysfunction in order to enhance clinical results. Microalbuminuria, sometimes referred to as proteinuria or elevated urine protein, is a sign of renal failure that can be detected using a dipstick test for urine or random spot urine analysis.

Aims/ objective: To compare pre and post anaesthetic urinary protein in patients of chronic kidney disease undergoing abdominal surgery under general anaesthesia.

Materials and Method: 50 patients of chronic kidney disease planned for elective abdominal surgery were enrolled in our study. Spot urine samples from patients were taken and preserved at - 20 degrees Celsius after being centrifuged and placed in sterile urine containers. One ml of a spot sample was combined with 20 ml of reagent-grade water for the measurement of urine creatinine. Urine samples for UPCR (urine protein creatinine ratio) and UACR (urine albumin creatinine ratio) were sent before anaesthesia, after surgery and 24 hours after anaesthesia. Serum creatinine was also measured and eGFR was calculated using Cockcroft-Gault equation.

Results: There was no significant rise in urine protein-creatinine ratio (UPCR) after surgery but the rise in UPCR was significant after 24 hours of anaesthesia ($p<0.001$). The rise in urine albumin-creatinine ratio (UACR) was more significant than rise in UPCR just after surgery. As compared to proteinuria, decline in eGFR (estimated by serum creatinine) was more pronounced and more significant. There was some improvement in eGFR values after 24 hour of anaesthesia as compared to post-operative values but the decline was still significant as compared to pre-operative values ($p<0.0001$).

Conclusion: There was significant decline in renal function with respect to proteinuria and eGFR in patients of chronic kidney disease undergoing elective abdominal surgery under general anaesthesia.

Keywords: Proteinuria, Chronic Kidney Disease, General Anaesthesia, eGFR, UPCR, UACR.

INTRODUCTION

With a predicted 8 to 16% global incidence, chronic kidney disease (CKD) is a widespread condition. As it progresses, it is linked to negative consequences like higher mortality from cardiovascular disease, a lower quality of life, and a shorter lifespan. [1-3]

The extent of proteinuria, the existence of arterial hypertension, and the GFR (glomerular filtration rate) at the moment of diagnosis are all directly connected to the deterioration in the functioning of the kidneys. By triggering several genes that code for vasoactive and pro-inflammatory mediators, protein molecules that are filtrated through the glomerular capillaries cause direct toxic damage to the tubulointerstitial structures, which, when combined with different risk factors like elevated blood pressure, accelerates the deterioration of the renal function. [4]

Hence, proteinuria is an important predictor for the GFR to fall more quickly. In a study of 352 non-diabetic patients of kidney disease, Ruggenenti et al. found that patients who had proteinuria above 3.9 g/24 h at the point of diagnosis had a stronger correlation with a reduction in GFR than patients with proteinuria less than 1.9 g/24 h and greater proportions of patients with elevated proteinuria developed end-stage renal disease (ESRD). [5] A further study found that as urine protein levels raised the risk of developing ESKD also risen, turning into significant for levels of 0.5 to 1 g per 24 h (HR of 1.8 and 1.85 in diabetic and non-diabetic patients, respectively) and more than 1 g (HR of 2.70 and 2.69 in diabetic and non-diabetic patients).[6]

According to a recently done meta-analysis of 28 research studies, a 30% decrease in proteinuria over a 2-year follow-up time was linked to a 22 percent lower chance of developing ESRD. [7] Hence, a better renal prognosis was linked to a decrease in urine protein levels in patients of glomerular renal disease. A higher risk of death,

coagulation disorders, thromboembolic conditions, bleeding from the gastrointestinal tract, cardiovascular disease, and stroke is also linked to elevated urine protein levels. [8]

Multiple factors, including hypovolemia, low systemic vascular resistance brought on by anaesthesia or compression of inferior vena cava, and direct disruption to the urinary system during surgical procedures, are known to increase the risk of post-operative acute kidney injury. Key predictors of post-operative AKI include factors that increase the length of renal ischemia and intra-operative hypotension. An analysis of the literature from 1952 to 2017 was undertaken by the peri-operative quality initiative in 2018, and the results showed that an intra-operative MAP below 60–70 mmHg was linked to an elevated risk of acute kidney injury and mortality. [9]

Accordingly, it seems that the incidence of acute kidney injury after surgery has not altered considerably over the past few decades, in spite of substantial advances in surgical methods, anaesthetic procedures, and critical care management. [10] In recent years, surgeons have started to explain how pre-operative risk factors and surgical acute kidney injury are related.

eGFR is typically used to calculate kidney function throughout pre-operative risk evaluations. According to KDIGO (Kidney Disease Improving Global Outcomes), novel approaches, such as the utilization of biomarkers to determine the likelihood of acute kidney injury are required to more accurately identify pre-operative renal dysfunction in order to enhance clinical results.[11] Microalbuminuria, sometimes referred to as proteinuria or elevated urine protein, is a sign of renal failure that can be detected using a dipstick test for urine or random spot urine analysis. [12, 13]

Given links with cardiovascular disease and mortality from all causes, research have historically used pre-operative urine protein levels measurements to forecast post-operative outcomes in cardiac, urological, and organ transplant surgery. [14-19] A very few studies assessing changes in proteinuria after general anaesthesia. So, this study was planned to compare pre and post anaesthetic urinary protein in patients of chronic kidney disease undergoing abdominal surgery under general anaesthesia.

MATERIALS AND METHODS

This was a comparative observational and prospective study conducted in department of anaesthesiology in collaboration with department of biochemistry in tertiary care hospital of eastern India from January 2023 to June 2023. Patients of chronic kidney disease planned for elective abdominal surgeries were recruited in the study after screening for eligibility criteria and taking written informed consent. Rights and safety of study participants were taken care of as per principles of Declaration of Helsinki and Good Clinical Practice.

Consecutive sampling method was used and all patients meeting our eligibility criteria during the study period were enrolled in the study.

Inclusion Criteria: Patients of either sex of age greater than 18 years diagnosed with grade 3-4 chronic kidney disease; patients being planned for elective abdominal surgeries under general anaesthesia; patients with moderately increased proteinuria having urine protein-creatinine ratio between 150 to 500 mg/g and Patients of ASA (American Society of Anaesthesiologist (ASA) physical status 1 to 2 were included in our study.

Exclusion Criteria: Patients allergic to any pre-anaesthetic medication or sevoflurane; pregnant or lactating women, patients on dialysis, patients having sign and symptoms of sepsis; or patients with any hepatic or cardiovascular diseases were excluded from our study.

45 minutes before the surgical procedure, atropine and midazolam were administered intramuscularly (IM) at doses of 0.01 and 0.07 mg per kg, respectively. While an intravenous (IV) line was inserted into an ante-cubital vein to determine the mean arterial blood pressure (MAP), heart rate (HR), and level of oxygen saturation in the peripheral circulation (SpO2), crystalloid infusion was started in the operation room. Tramadol and sevoflurane alongside a fresh gas flow of 2 L/min were utilized to maintain the anaesthesia, which was induced with propofol at a dose of 2 mg per kg and atracurium at a dose of 0.5 mg per kg. In order to keep the patients' end-expiratory CO_2 level within 34- and 36-mm Hg, patients were put on mechanical ventilation. After surgery, neostigmine at a dose of 1.5 mg and atropine at a dose of 0.5 mg were administered to treat neuromuscular block. Patients were moved to the surgical recovery unit following tracheal extubation.

Spot urine samples from patients were taken and preserved at - 20 degrees Celsius after being centrifuged and placed in sterile urine containers. One ml of a spot sample was combined with 20 ml of reagent-grade water for the measurement of urine creatinine. All study participants' urine protein and creatinine levels were estimated using the Vitros 5.1 Fusion chemistry device manufactured by Orthoclinical Diagnostics by Johnson and Johnson (USA). Urine samples for UPCR (urine protein creatinine ratio) and UACR (urine albumin creatinine ratio) were sent before anaesthesia, after surgery and 24 hours after anaesthesia. Serum creatinine was also measured and eGFR was calculated using Cockcroft-Gault equation.

Statistical Analysis: Data collected at baseline, before surgery and after surgery were compiled in a tabular form using Microsoft Excel 365 and transferred to SPSS version 24 for statistical analysis. Continuous data such as age, duration of chronic kidney disease, UPCR, UACR, and eGFR were expressed as mean ± standard deviation (SD) and paired t test was used to evaluate statistical significance of difference between pre and post anaesthetic values with

p-value of less than 0.05 as indicator of statistical significance.

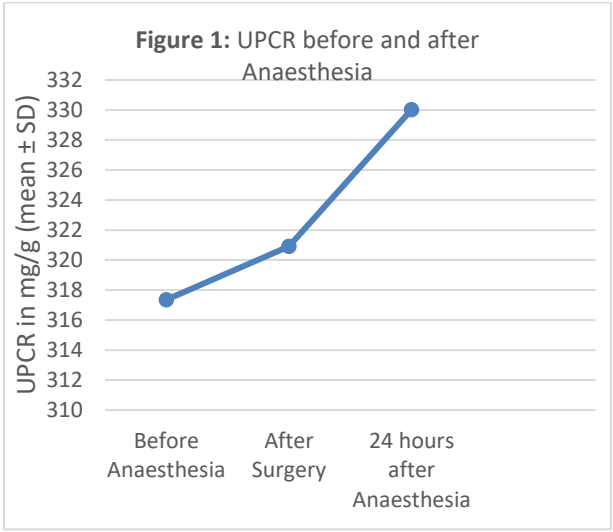
RESULTS

50 patients of chronic kidney disease planned for elective abdominal surgery meeting our eligibility criteria were enrolled in our study. Their baseline demographic and clinical characteristics are given is given in Table 1.

Table 1: Baseline demographic and clinical characteristics of patients before surgery

Variables	Values
Age in years (mean ± SD)	53.33 ± 7.44
Duration of chronic kidney disease in years (mean ± SD)	0.75 ± 0.32
Duration of Surgery in minutes (mean ± SD)	98.85 ± 9.17
Gender, n (%)	
Male	23 (46.00)
Female	27 (54.00)
ASA physical status, n (%)	
1	32 (64.00)
2	18 (36.00)
Grade of CKD	
3a	29 (58.00)
3b	14 (28.00)
4	7 (14.00)

Most of the patients with chronic kidney disease in our study belonged to age group of 40-60 years. There were slightly greater proportion of female CKD patients undergoing elective abdominal surgery. Most of the study participants were having grade 3a CKD of ASA status 1.



There was no significant rise in urine protein-creatinine ratio (UPCR) after surgery but the rise in UPCR was significant after 24 hours of anaesthesia (p<0.001).

Table 2: Comparison of urine protein-creatinine ratio (UPCR) before and after anaesthesia (n = 50)

	Before Anaesthesia	After Surgery	P-Value (Paired t test)
UPCR in mg/g (mean ± SD)	317.35 ± 44.10	320.91 ± 54.42	0.12
	Before Anaesthesia	24 hours after anaesthesia	P-Value (Paired t test)
UPCR in mg/g (mean ± SD)	317.35 ± 44.10	330.02 ± 44.21	<0.001
P-Value (Repeated measure ANOVA): <0.001			

Table 3: Comparison of urine albumin-creatinine ratio (UACR) before and after anaesthesia

	Before Anaesthesia	After Surgery	P-Value (Paired t test)
UACR in mg/g (mean ± SD)	109.55 ± 18.25	111.36 ± 22.98	0.03
	Before Anaesthesia	24 hours after anaesthesia	P-Value (Paired t test)
UACR in mg/g (mean ± SD)	109.86 ± 17.31	115.18 ± 16.76	<0.001
P-Value (Repeated measure ANOVA): <0.001			

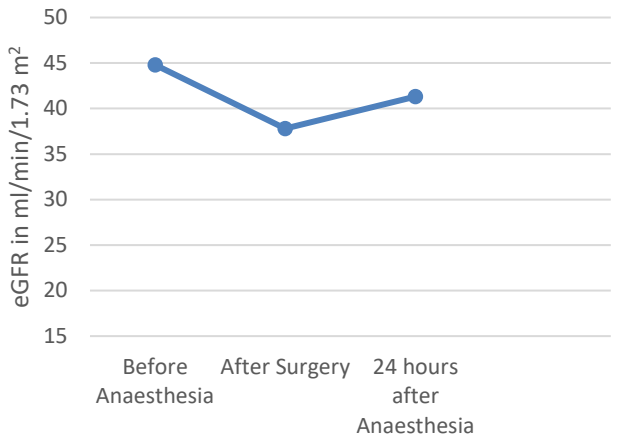
The rise in urine albumin-creatinine ratio (UACR) was more significant than rise in UPCR just after surgery.

Table 4: Comparison of eGFR before and after anaesthesia

	Before Anaesthesia	After Surgery	P-Value (Paired t test)
eGFR in ml/min/1.73 m^2	44.80 ± 10.54	37.80 ± 11.24	<0.0001
	Before Anaesthesia	24 hours after anaesthesia	P-Value (Paired t test)
eGFR in ml/min/1.73 m^2 (mean ± SD)	44.80 ± 10.54	41.30 ± 10.89	<0.0001
P-Value (Repeated measure ANOVA): <0.0001			

As compared to proteinuria, decline in eGFR (estimated by serum creatinine) was more pronounced and more significant. There was some improvement in eGFR values after 24 hours of anaesthesia as compared to post-operative values but the decline was still significant as compared to pre-operative values (p<0.0001).

Figure 2: eGFR before and after Anaesthesia



DISCUSSION

In this single-cantered observational and prospective study done on patients of chronic kidney disease undergoing elective abdominal surgery under general anaesthesia, we noted significant decline in renal function with respect to proteinuria and eGFR. The patients with moderately increased proteinuria having urine protein-creatinine ratio between 150 to 500 mg/g were included in the study to detect impact of anaesthesia and surgery on already developed pathological process of proteinuria. Patients with severely increased proteinuria and grade 5 CKD patients were excluded to avoid any risk involved in the study.

The rise in UPCR from 317.35 to 320.91 was not statistically significant as compared to rise in UACR from 109.55 to 111.36 which was statistically significant. UACR and UPCR are not directly comparable, hence CKD guidelines have different views on choosing between the two parameters in different clinical scenario.[20] For instance, the Caring for Australians with Renal Impairment Guidelines, the Scottish Intercollegiate Guidelines Network, and the UK CKD guidelines all advise using UACR for patients with diabetes mellitus and UPCR for patients having non-diabetic chronic kidney disease.[20] In contrast, UPCR is considered appropriate if the UACR is substantially elevated, while the Kidney Disease Quality Outcomes Initiative Guidelines encourage UACR. [20]

Given that albuminuria serves as a surrogate criterion for early diabetic nephropathy in patients with diabetes, it should be preferred in diabetic patients.[21] Asians with diabetes actually have the greatest frequency of albuminuria (55 percent) globally, making the need for screening of UACR even more crucial.[22] Additionally, UACR is a more accurate indicator of CKD than UPCR. In a cross-sectional survey at community level, 8 percent of people with proteinuria (particularly non-diabetics) had no albuminuria, whereas 67.5 percent of subject with albuminuria were found to have normal UPCR, according to a direct comparative research.[23] Therefore, 67.5 percent of patients with albuminuria for whom therapy with angiotensin receptor blockers is financially advantageous could have been missed by assessing only UPCR. For those who have established proteinuria, there is no need to assess UACR.

Due to certain factors, screening of UPCR is suggested to be performed in patients who are not diabetic. Test for UPCR is less expensive than test for UACR. [24] Second, elevated UPCR levels rather than UACR level was detected in the majority of reno-protective randomized controlled trials in non-diabetic patients and in many RCTs UPCR was used as a treatment outcome (in both deiabetic and non-diabetic patients).[20] Third, only patients with proteinuria greater than 0.5 g/24-hour benefit from ACE inhibitors in terms of decreasing the advancement of chronic kidney disease. [25] In a nutshell, ACE inhibitors are ineffective for people who do not have diabetes but have microalbuminuria. Last but not least, glomerulonephritis, a condition that causes non-diabetic chronic kidney disease is defined by proteinuria rather than albuminuria, and is still widespread in Asian countries. Fortunately, as a result of universal proteinuria screening, its frequency has reduced in Japan. [26]

Pre-operative kidney dysfunction has been linked to unfavourable consequences after surgery, such as acute kidney injury and readmission, which is in agreement with our findings. [27, 28] Pre-operative renal dysfunction with an inadequate eGFR (less than 60 mL/min/1.73 m2) was related with acute kidney injury within 1 month and both immediate and long-term mortality, according to Mooney et al.'s systematic review and meta-analysis of cardiac and vascular surgery.[28] Comparable findings have been observed in studies of pre-operative renal dysfunction in noncardiac, nontransplant surgical settings. According to an analysis of 39,989 subjects by Blitz and colleagues, pre-operative impaired renal function, as determined by eGFR classifications for chronic kidney disease, and proteinuria was linked to both acute kidney injury and unexpected surgical recalls.[27]

The above findings are supported by our results, which indicates that pre-operative proteinuria, not dependent on preoperative renal impairment, is has positive correlation with decline in eGFR. Patients with elevated UPCR and UACR with low eGFR are more likely to develop acute kidney injury than those with low eGFR but low UPCR or UACR.

A urine dipstick urine analysis is recommended to be used to check for proteinuria in diabetic patients, black race, patients with CKD, patients with functional dependency, and many co-morbid conditions. Although pre-operative urine analysis screenings for proteinuria can potentially be helpful for all patients planned for surgical procedures, proteinuria has been estimated to impact between 8 percent and 33 percent of the population in general. [29-31] Given that proteinuria might appear before deterioration in eGFR and serum creatinine level, conducting pre-operative dipstick urinalysis for proteinuria which has 96% sensitivity and 87% specificity,[32] could prove to be an effective method for determining the possibility of acute kidney injury after surgery.

CONCLUSION

There was significant decline in renal function with respect to proteinuria and eGFR in patients of chronic kidney disease undergoing elective abdominal surgery under general anaesthesia. Pre-operative urine analysis for proteinuria and albuminuria should be promoted and used as indicator of intra-operative and post-operative risk and outcomes. Long term studies with more sample size and multicentric design should be conducted to evaluate and compare the effect of different anaesthetic techniques and surgical procedures on renal function to generate optimum evidence for clinicians and surgeons.

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