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EFFECTIVENESS OF N-ACETYLCYSTEINE AND TAURINE IN REDUCING MICROALBUMINURIA IN DIABETIC AND HYPERTENSIVE PATIENTS WITH CHRONIC KIDNEY DISEASE: A RETROSPECTIVE, OBSERVATIONAL STUDY

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ABSTRACT

Background: Microalbuminuria is one of the earliest signs and a major risk factor for chronic kidney disease (CKD) progression, often aggravated by the concomitant presence of diabetes and/or hypertension. One of the major pathophysiological contributors to CKD is oxidative stress. The current study investigated the effectiveness of combination therapy with antioxidants N-acetylcysteine (NAC) and Taurine in reducing urinary albumin to creatinine ratio (uACR). **Methods:** In this retrospective study, data were analyzed from 305 adult diabetic and/or hypertensive patients diagnosed with CKD stage 1-3. All patients had microalbuminuria (uACR: 30-300mg/g) and were treated with NAC (150mg) + Taurine (500mg) (Nefrosave®) as an adjuvant therapy. The primary and secondary outcome measures included changes in uACR and the incidence of adverse events, respectively, from baseline to Day 90 of treatment. **Results:** The overall mean uACR reduced significantly from 131.13mg/g to 115.69mg/g (11.77%, p<0.001) after 90 days of treatment with NAC+Taurine. Reduction in mean uACR was also evident in subgroups of patients with both diabetes and hypertension (11.15%, p<0.001), diabetes alone (15.09%, p<0.001), and hypertension alone (8.31%, p=0.561), as well as amongst patients with CKD stage 1 (16.77%, p=0.002), stage 2 (14.45%, p<0.001) and stage 3 (5.19%, p=0.003). No adverse events were reported. **Conclusion:** The combination of NAC and Taurine could be an effective nephroprotective adjuvant therapy in reducing microalbuminuria in diabetic and/or hypertensive adult patients with CKD stage 1-3; Outcome was found to be better when treatment was initiated early.

KEYWORDS: Chronic kidney disease (CKD), Microalbuminuria, N-acetylcysteine, Taurine, Diabetes, Hypertension.

INTRODUCTION

Chronic kidney disease (CKD) is defined as 'abnormalities of kidney structure or function, present for a minimum of 3 months, with implications for health'.[1] Although majority of the diagnosed cases worldwide are in late stages of the disease, individuals with early-stage CKD often remain undiagnosed as they are mostly clinically asymptomatic. Untreated early-stage CKD might advance to develop complications or end stage renal disease (ESRD). This progression might be accelerated in individuals with diabetes, hypertension, or obesity as these are modifiable risk factors for CKD.[2] Given the high burden of these non-communicable metabolic disorders in the country[3], it is comprehensible why India is one of the two nations that contribute to one-third of CKD patients globally, the other nation being China.[4,5] Early intervention of CKD is, therefore, of paramount importance.

The KDIGO 2024 clinical practice guidelines for the evaluation and management of CKD include the use of renin-angiotensin system inhibitors (RASi) (angiotensin-converting enzyme inhibitor (ACEi) or angiotensin II receptor blocker (ARB)), sodium-glucose cotransporter-2 inhibitors (SGLT2i), mineralocorticoid receptor antagonists (MRA), and glucagon-like peptide-1 receptor agonists (GLP-1 RA) depending on comorbidities in patients.[1,6] Pathophysiological mechanisms of CKD involve mitochondrial dysfunction resulting in oxidative stress (OS) which is one of the non-traditional risk factors that perhaps contributes to the cardiovascular burden in CKD patients. Progression of renal injury is associated with OS-triggered elevation in inflammatory markers leading to renal fibrosis, while vascular endothelial injury is associated with high levels of homocysteine (HCY) and uremic toxin. Antioxidative treatment for reduction of OS is, therefore, a relatively novel treatment strategy to manage CKD progression.[7,8] N-acetylcysteine (NAC) and Taurine are two of the antioxidants reported to play roles in renal functions. NAC is a thiol compound (acetylated precursor of L-Cysteine and reduced glutathione) that reduces the production of oxygen free radicals and the levels of pro-inflammatory cytokines. Taurine is a conditionally essential amino acid that functions as an intracellular osmolyte.[7,9]

A meta-analysis of 15 randomized trials by Ye *et al.* showed that NAC reduced cardiovascular events among CKD patients and that estimated glomerular filtration rate (eGFR) and serum creatinine were significantly better when treated with NAC compared to placebo.[7] Results from a retrospective study in a large cohort of over 100,000 CKD patients followed for 10 years showed that use of NAC was associated with a significant 18% reduction in the risk for ESRD, with renal protective effects evident after 90 days.[10] Similar conclusions were drawn in a 3-year retrospective study, which attributed the beneficial effects of NAC to modulation of serum creatinine and eGFR.[11] NAC has also been shown to improve residual renal function in patients undergoing dialysis.[12] Although the exact mechanisms of NAC-conferred renal protection remain elusive, evidence suggests that NAC reduces serum creatinine levels, increases the clearance of endogenous creatinine, improves the ultrastructure of podocytes thus delaying the deterioration of renal function, replenishes glutathione levels that gets depleted in CKD, acts as a source of sulfhydryl groups and a scavenger of free radicals, and that this widely-used compound is well-tolerated and has no serious side effects.[7,10,11,13] Likewise, Taurine has been shown to exert cytoprotective effects on the homeostasis of renal cells due to its antioxidant and osmoregulatory properties, positively affecting ion reabsorption and secretion, urine composition, renal blood flow, and glomerular filtration although the exact mechanisms of Taurine-mediated protection against CKD progression is not delineated.[9,14,15]

Since reactive oxygen species (ROS) are known to damage the glycocalyx within the glomerular filtration barrier (GFB) thus causing proteinuria[16], a combination of antioxidants is expected to be beneficial and GFB has been proposed as a structural target for novel kidney therapies.[17] We aimed to evaluate the effectiveness of the nephroprotective combination of NAC+Taurine in management of microalbuminuria that is a critical risk factor for CKD progression, especially in the concomitant presence of diabetes or hypertension[16], as well as one of the earliest signs of the condition. Previous studies pointed to a beneficial effect of this combination in CKD patients.[18,19] The current study assessed real-world evidence on the supplementation of NAC+Taurine in diabetic and/or hypertensive patients with CKD.

METHODS

Study design

This retrospective study was conducted using electronic medical records (EMRs) of CKD patients treated with twice-daily dose of 150mg NAC + 500mg Taurine (Nefrosave® tablet from Fourrts India Laboratories) between October 2022 and October 2023. EMRs were retrieved from nine physicians based in geographically-diverse regions across India (Chennai, Kolkata, Mumbai, Ahmedabad).

Patient characteristics

A total of 320 EMRs of adult CKD patients were screened, out of which 305 fulfilled study eligibility criteria and were included for analysis. Included patients (male, 194; female, 111) had comorbidities (diabetes and hypertension, 197; diabetes, 80; hypertension, 28) and were diagnosed with CKD stage 1-3 (stage 1, 75; stage 2, 107; stage 3, 123) based on eGFR evaluated using creatinine levels. All patients had microalbuminuria (uACR: 30-300mg/g) and were prescribed NAC+Taurine as an adjuvant therapy along with low-protein diet as mentioned in EMRs. Patients with incomplete medical records regarding the required study parameters were excluded.

Outcome measures

The primary outcome measure was the change in urinary albumin to creatinine ratio (uACR) from baseline till 90 days amongst all patients and in different subgroups. The secondary outcome measure was the incidence of adverse events.

Ethical conduct of the study

All study procedures conformed to the clinical study protocol approved by an independent ethics committee. Permission for a waiver of informed patient consent was obtained per the ICMR 2017 guidelines since this study involved extracting aggregate data from EMRs and analyzing it in an anonymized manner. Patient confidentiality was maintained throughout. The trial was registered with the Clinical Trials Registry-India (CTRI) on 20 December 2023 (reference number: CTRI/2023/12/060567).

Statistical methods

As per Viswanathan et al., treatment of patients with NAC+Taurine for 3 months decreased uACR by approximately 50%.[19] Therefore, a sample size of at least 300 is required to observe a similar reduction in uACR with 95% confidence interval and 5.7% margin of error. All statistical methods were based on the International Council for Harmonization E9 document ‘Statistical Principles for Clinical Trials’ and analyses were done using Statistical Package for Social Science (SPSS) version SPSS 28.0.1.1 (IBM Corp., Armonk, NY, USA). $p<0.05$ was considered statistically significant. Wilcoxon signed-rank test was used to compare uACR.

RESULTS

The mean ± SD age of patients was 61.87 ± 10.77 years, and the majority were male (63.60%). The proportion of patients with CKD stage 1, 2, and 3 (based on physician's serum creatinine-based eGFR calculations) was 54.59%, 35.08%, and 40.33%, respectively. The proportion of patients with both diabetes and hypertension was higher (64.59%) in comparison to that with either diabetes (26.23%) or hypertension (9.18%) **(Table 1)**. Comorbidities like dyslipidemia, hypothyroidism, hypercholesterolemia, etc. were each noted in fewer than 30% patients. Concomitant consumption of antidiabetic medication was noted in 59.65% patients, antihypertensives in 53.78%, and cholesterol-lowering medications in 49.51%.

Change in uACR

After 90 days of treatment with NAC+Taurine, the overall mean ± SD uACR reduced from 131.13 ± 81.76 mg/g to 115.69 ± 88.62 mg/g, resulting in a significant decrease by 15.44 mg/g (11.77%; p<0.001). The decrease in mean uACR was also statistically significant in subgroups of patients with diabetes (15.09%; p<0.001) and with both diabetes and hypertension (11.15%; p<0.001). Patients with hypertension also showed decrease in mean uACR (8.31%; p=0.561) **(Table 2 and Figure 1)**. Significant decreases in mean uACR were observed in all CKD patients analyzed (p<0.05 in all cases; **Table 2 and Figure 2)**:

- Stage 1 (16.77%; p=0.002),
- Stage 2 (14.45%; p<0.001),
- Stage 3 (5.19%; p=0.003).

Change in eGFR and serum creatinine

Data on post-treatment eGFR levels was available for 233 patients while that for serum creatinine was available for 251 patients. Results showed that the mean ± SD eGFR changed from 73.77 ± 22.01 ml/min/1.73m^2 at baseline to 74.39 ± 21.40 ml/min/1.73m^2 at Day 90 (p=0.384). The mean ± SD serum creatinine changed from 1.16 ± 0.41 mg/dl at baseline to 1.15 ± 0.43 mg/dl at Day 90 (p=0.151).

Safety analysis: No adverse events were reported in any patient during the duration of treatment.

Table 1: Baseline characteristics of patients (N=305).

Age (years)	
Mean ± SD	61.88 ± 10.77
Median (min, max)	62.00 (30.00, 87.00)
Height (cm)	
Mean ± SD	160.91 ± 7.74
Median (min, max)	162.00 (134.00, 178.00)
Weight (kg)	
Mean ± SD	70.34 ± 13.02
Median (min, max)	69.00 (36.00, 138.50)
Pulse rate (beats per min)	
Mean ± SD	81.98 ± 8.77
Median (min, max)	80.00 (52.00, 118.00)
Sex, n (%)	
Male	194 (63.60%)
Female	111 (36.40%)
Systolic Blood Pressure (SBP; mmHg)	
Mean ± SD	130.10 ± 15.80
Median (min, max)	130.00 (90.00, 180.00)

Diastolic Blood Pressure (SBP; mmHg)	
Mean ± SD	77.00 ± 9.26
Median (min, max)	80.00 (50.00, 108.00)
Stage of CKD, n (%)	
Stage 1	75 (24.59%)
Stage 2	107 (35.08%)
Stage 3	123 (40.33%)
Comorbidity, n (%)	
Type 2 diabetes and hypertension	197 (64.59%)
Type 2 diabetes	80 (26.23%)
Hypertension	28 (9.18%)

Table 2: Change in uACR (mg/g) after 90 days of NAC+Taurine treatment.

	Baseline	Day 90	Mean change	p-value
Overall analysis (N=305)				
Mean ± SD	131.13 ± 81.76	115.69 ± 88.62	-15.44 (-11.77%)	<0.001***
Median (min, max)	112 (30, 299)	94 (2.72, 555)		
Patients categorized by comorbidity				
Diabetes (n=80)				
Mean ± SD	115.67 ± 80.95	98.21 ± 69.96	-17.46 (-15.09%)	<0.001***
Median (min, max)	95 (30.10, 299)	82.65 (3.80, 290)		
Hypertension (n=28)				
Mean ± SD	147.82 ± 86.28	135.54 ± 100.97	-12.28 (-8.31%)	0.561
Median (min, max)	130 (35, 299)	119.66 (18, 365.97)		
Diabetes and Hypertension (n=197)				
Mean ± SD	135.04 ± 80.92	119.97 ± 92.94	-15.07 (-11.15%)	<0.001***
Median (min, max)	116 (30, 299)	98.45 (2.72, 555)		
Patients categorized by stage of CKD				
Stage 1 CKD (n=75)				
Mean ± SD	142.84 ± 81.56	118.89 ± 75.94	-23.95 (-16.77%)	0.002**
Median (min, max)	130 (38.20, 299)	110 (3.80, 365.97)		
Stage 2 CKD (n=107)				
Mean ± SD	140.55 ± 80.90	120.24 ± 87.30	-20.31 (-14.45%)	<0.001***
Median (min, max)	130 (30.49, 299)	110 (2.72, 516)		
Stage 3 CKD (n=123)				
Mean ± SD	115.79 ± 80.93	109.78 ± 96.90	-6.01 (-5.19%)	0.003**
Median (min, max)	90 (30, 299)	79 (8.56, 555)		

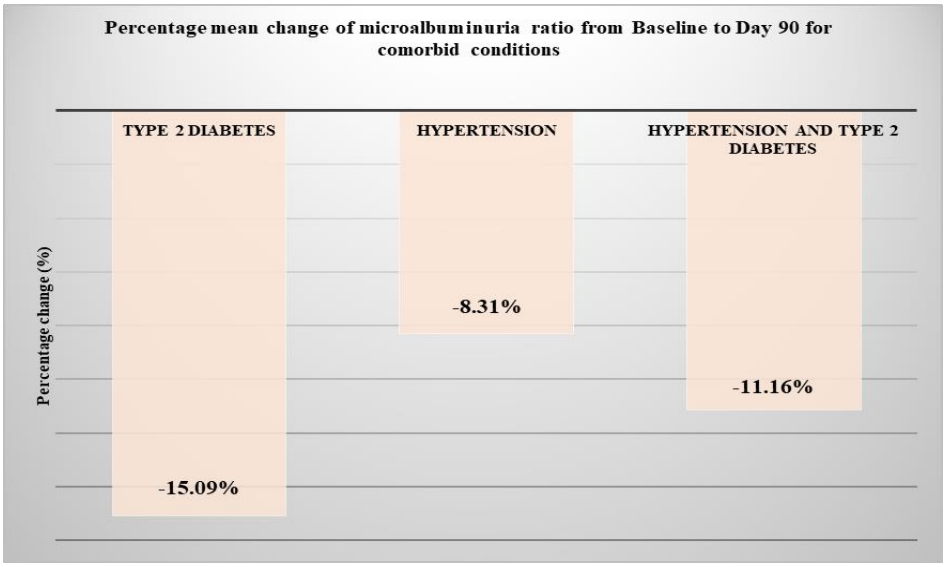

Figure 1: Change in uACR from baseline to Day 90: Treatment response in diabetic and hypertensive CKD patients.

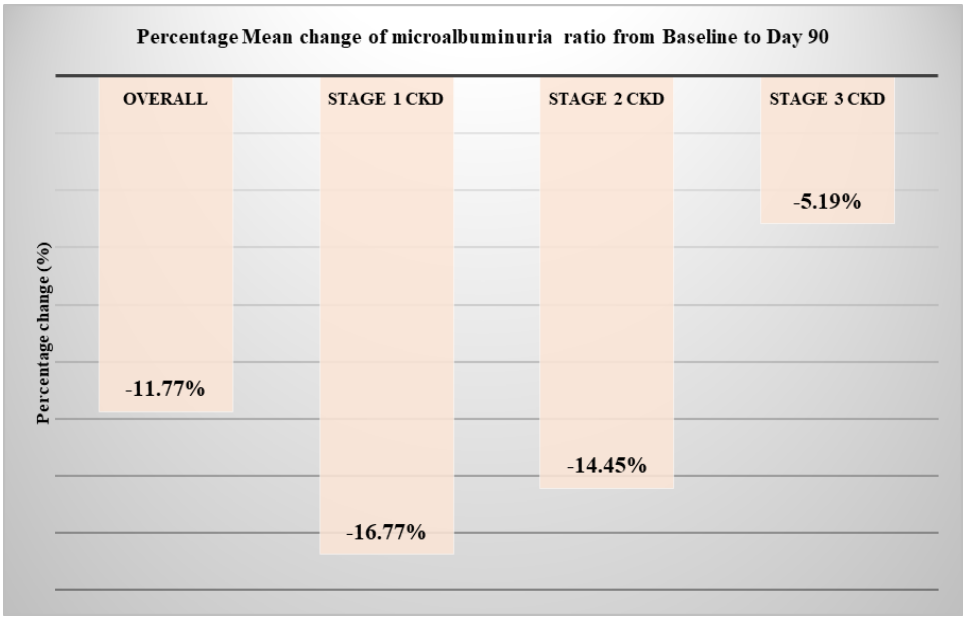

Figure 2: Change in uACR from baseline to Day 90: Treatment response in patients with CKD stage 1, 2, and 3

DISCUSSION

Meta-analysis of published clinical trials showed that antioxidant therapy significantly reduces development of ESRD and kidney failure in CKD patients.[20–22] While Jun *et al.* reported lowering of serum creatinine levels and improvement in creatinine clearance[21], Colombijn *et al.* reported little to no effect on uACR, serum creatinine, and eGFR.[20] Most studies included in these meta-analyses were conducted on patients with advanced-stage CKD (stage 3 and beyond) or patients on dialysis or transplant.[20–22] We believe that there is limited appreciation for antioxidant therapy in CKD perhaps due to a dearth of studies on patients with early-stage CKD despite being known that interventions at early stages have better prognostic values. This, in turn, is perhaps because very few patients are diagnosed in initial stages of the disease. The current study benefitted from the availability of data in patients with CKD stage 1, 2, and 3 as it allowed evaluation of the effect of antioxidants NAC+Taurine on uACR in early-stage CKD.

Results from the current retrospective study showed that the decrease in mean uACR upon treatment with NAC+Taurine was statistically significant in all patients of CKD stage 1-3, as well as in subgroups of patients at each stage. This reinforces the well-established fact that earlier initiation of CKD treatment leads to better outcomes. Similar conclusions were made by Sengupta *et al.* in a study wherein a subgroup of patients with comparatively earlier-stage CKD had better treatment outcome than the rest of the cohort.[23] The current study further showed that NAC+Taurine was effective in lowering uACR in CKD patients with concomitant conditions of diabetes, hypertension, or both; the effect was statistically significant in patients with diabetes and in those with both diabetes and hypertension. Further, it was noted that among the diabetic and/or hypertensive patients included in this study, only 137/305 (44.92%) were on ACEi/ARB and 77/305 (25.25%) were on SGLT2i/GLP-1 RA as per the recent recommendations by KDIGO.[1,6] Analysis of uACR levels revealed that patients in both these subgroups showed a greater decrease from baseline to Day 90 [ACEi/ARB, -16.92 (-12.46%); SGLT2i/GLP-1 RA, -19.10 (-14.20%)] compared to findings of the overall analysis [-15.44 (-11.77%)] in all 305 patients. Hence, supplementation with NAC+Taurine alongside recommended treatments

in diabetic and/or hypertensive patients is expected to facilitate improvement in their condition of CKD. Mean eGFR and serum creatinine levels at Day 90 were similar to corresponding values at baseline.

In non-diabetic early-stage CKD patients (n=19), Renke *et al.* reported no significant changes in uACR after NAC treatment for 8 weeks as compared to placebo.[24] A study on a small cohort of 10 patients showed that microalbuminuria reduced from 72 ± 16 µg/min to 68 ± 18 µg/min after 12 months of treatment with Taurine.[25] A prospective study in 60 CKD patients showed non-significant increase in albuminuria upon treatment with NAC or NAC+Taurine for 24 weeks. However, without further information on stage of CKD in these patients, it is difficult to interpret the treatment outcome.[26] In diabetic patients treated with NAC+Taurine for 3 months, a statistically significant decrease in uACR was observed by Viswanathan *et al.* from 85 ± 59 mg/mg to 45 ± 25 mg/mg (n=31; p=0.001)[19] while Premanath *et al.* observed a non-significant decrease in uACR from 161.75 mcg to 138.42 mcg (n=41).[18] Taken together, results from earlier studies do suggest a beneficial effect of NAC+Taurine in CKD. Potential reasons of non-significant results in some of these studies, as pointed out by the respective authors, might be low sample size or low dosage of treatment.

The current study presents evidence of NAC+Taurine treatment in diabetic and hypertensive patients. However, limitations of the study are low sample size and short duration of treatment. Since this study reports real-world data on Indian patients, the results might not be generalizable to patients elsewhere in the world due to variation in ethnicity, genetic predispositions, dietary habits, etc. The current cohort of patients were not just administered NAC+Taurine, but consumed concomitant medications for other conditions apart from CKD. A cumulative effect of all medications should ideally be taken into consideration to comment on the status of diabetes/hypertension and CKD in these patients; such analysis was beyond the scope of this retrospective study. Prospective randomized controlled studies involving long-term follow-up of larger patient cohorts are necessary to support the findings from this study.

Overall, results from this study showed that a combination of NAC (150mg) and Taurine (500mg) might be an effective and safe nephroprotective adjuvant therapy for diabetic and/or hypertensive CKD patients with microalbuminuria. These findings support the supplementation of NAC+Taurine in early-stage CKD for favorable treatment outcomes.

REFERENCES

1. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int*., 2024; 105(4S): S117-S314. doi:10.1016/j.kint.2023.10.018
2. Evans M, Lewis RD, Morgan AR, et al. A Narrative Review of Chronic Kidney Disease in Clinical Practice: Current Challenges and Future Perspectives. *Adv Ther*, 2022; 39(1): 33-43. doi:10.1007/s12325-021-01927-z
3. Anjana RM, Unnikrishnan R, Deepa M, et al. Metabolic non-communicable disease health report of India: the ICMR-INDIAB national cross-sectional study (ICMR-INDIAB-17). *Lancet Diabetes Endocrinol*, 2023; 11(7): 474-489. doi:10.1016/S2213-8587(23)00119-5
4. Francis A, Harhay MN, Ong ACM, et al. Chronic kidney disease and the global public health agenda: an international consensus. *Nat Rev Nephrol*. Published online April 3, 2024. doi:10.1038/s41581-024-00820-6
5. GBD Chronic Kidney Disease Collaboration. Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*, 2020; 395(10225): 709-733. doi:10.1016/S0140-6736(20)30045-3.

6. Levin A, Ahmed SB, Carrero JJ, et al. Executive summary of the KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease: known knowns and known unknowns. *Kidney Int*, 2024; 105(4): 684-701. doi:10.1016/j.kint.2023.10.016.
7. Ye M, Lin W, Zheng J, Lin S. N-acetylcysteine for chronic kidney disease: a systematic review and meta-analysis. *Am J Transl Res*, 2021; 13(4): 2472-2485.
8. Small DM, Coombes JS, Bennett N, Johnson DW, Gobe GC. Oxidative stress, anti-oxidant therapies and chronic kidney disease. *Nephrology (Carlton)*, 2012; 17(4): 311-321. doi:10.1111/j.1440-1797.2012.01572.x
9. Chesney RW, Han X, Patters AB. Taurine and the renal system. *J Biomed Sci*, 2010; 17 Suppl 1(Suppl 1): S4. doi:10.1186/1423-0127-17-S1-S4.
10. Liao CY, Chung CH, Wu CC, et al. Protective effect of N-acetylcysteine on progression to end-stage renal disease: Necessity for prospective clinical trial. *Eur J Intern Med*, 2017; 44: 67-73. doi:10.1016/j.ejim.2017.06.011
11. Chiu AH, Wang CJ, Lin YL, Wang CL, Chiang TI. N-Acetylcysteine Alleviates the Progression of Chronic Kidney Disease: A Three-Year Cohort Study. *Medicina (Kaunas)*, 2023; 59(11): 1983. doi:10.3390/medicina59111983.
12. Feldman L, Shani M, Sinuani I, Beberashvili I, Weissgarten J. N-acetylcysteine may improve residual renal function in hemodialysis patients: a pilot study. *Hemodial Int*, 2012; 16(4): 512-516. doi:10.1111/j.1542-4758.2012.00702.x.
13. Huang JW, Lahey B, Clarkin OJ, et al. A Systematic Review of the Effect of N-Acetylcysteine on Serum Creatinine and Cystatin C Measurements. *Kidney Int Rep*., 2021; 6(2): 396-403. doi:10.1016/j.ekir.2020.11.018.
14. Baliou S, Adamaki M, Ioannou P, et al. Ameliorative effect of taurine against diabetes and renal-associated disorders (Review). *Med Int (Lond)*, 2021; 1(2): 3. doi:10.3892/mi.2021.3.
15. Schaffer SW, Azuma J, Mozaffari M. Role of antioxidant activity of taurine in diabetes. *Can J Physiol Pharmacol*, 2009; 87(2): 91-99. doi:10.1139/Y08-110.
16. Singh A, Satchell SC. Microalbuminuria: causes and implications. *Pediatr Nephrol*, 2011; 26(11): 1957-1965. doi:10.1007/s00467-011-1777-1.
17. Daehn IS, Duffield JS. The glomerular filtration barrier: a structural target for novel kidney therapies. *Nat Rev Drug Discov*, 2021; 20(10): 770-788. doi:10.1038/s41573-021-00242-0.
18. Premanath M, Mahesh M, Babu Ms, Bhanukumar M, Devananda D. Can N acetyl cysteine - Taurine provide additional reduction in microalbuminuria in type 2 diabetic patients already on optimum doses of Angiotensin converting enzyme inhibitors? *Int J Health Allied Sci*., 2019; 8(4): 236. doi:10.4103/ijhas.IJHAS_27_19.
19. Viswanathan V, Nair MB, Tilak P. Effect of taurine and acetylcysteine in attenuating microalbuminuria in type 2 diabetes. *Indian J Nephrol*, 2008; 18(2): 85. doi:10.4103/0971-4065.42349.
20. Colombijn JM, Hooft L, Jun M, et al. Antioxidants for adults with chronic kidney disease. *Cochrane Database Syst Rev*, 2023; 11(11): CD008176. doi:10.1002/14651858.CD008176.pub3.
21. Jun M, Venkataraman V, Razavian M, et al. Antioxidants for chronic kidney disease. *Cochrane Database Syst Rev,* 2012; 10(10): CD008176. doi:10.1002/14651858.CD008176.pub2.
22. Casanova AG, López-Hernández FJ, Vicente-Vicente L, Morales AI. Are Antioxidants Useful in Preventing the Progression of Chronic Kidney Disease? *Antioxidants (Basel)*, 2021; 10(11): 1669. doi:10.3390/antiox10111669.
23. Sengupta P, Biswas S, Roy T. Comparative Study to Evaluate the Effect of Low-Protein Diet Supplementation with Taurine and N-Acetylcysteine, N-Acetylcysteine and Pyridoxamine Dihydrochloride in Preventing the Progression

of Chronic Renal Failure in Patients with Non-Diabetic Kidney Disease. *J Assoc Physicians India*, 2022; 70(5): 11-12.

24. Renke M, Tylicki L, Rutkowski P, et al. The effect of N-acetylcysteine on blood pressure and markers of cardiovascular risk in non-diabetic patients with chronic kidney disease: a placebo-controlled, randomized, cross-over study. *Med Sci Monit*, 2010; 16(7): PI13-18.
25. Nakamura T, Ushiyama C, Suzuki S, et al. Effects of taurine and vitamin E on microalbuminuria, plasma metalloproteinase-9, and serum type IV collagen concentrations in patients with diabetic nephropathy. *Nephron*, 1999; 83(4): 361-362. doi:10.1159/000045430
26. Singh A, Agarwal P, Kaushik S. Study to Compare the Therapeutic Efficacy of N-Acetyl Cysteine and Combination of N-Acetyl Cysteine and Taurine in Proteinuria in Diabetic Nephropathy. *Asian J Pharm Clin Res*, 2017; 10(2): 230-232. doi:10.22159/ajpcr.2017.v10i2.15369