EVALUATING URINARY HAPTOGLOBULIN AS A BIOMARKER FOR EARLY RENAL FUNCTION DECLINE IN T2DM

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Abstract: Background and Aims: Diabetic nephropathy (DN) affect a significant proportion of diabetes mellitus (T2DM) patients. Microalbuminuria, an early marker of diabetic kidney disease (DKD), has limited sensitivity and specificity, particularly in normoalbuminuric patients, where 38-73% with chronic kidney disease (CKD) lack microalbuminuria. Urinary haptoglobin (uHp) and its ratio with creatinine (uHCR) are emerging biomarkers for early detection of renal dysfunction. This study evaluates the diagnostic utility of uHCR in detecting and predicting renal function decline in T2DM.

Methods: This prospective analytical study was conducted at F.H. Medical College, Agra, India, with Ethical Committee approval and informed consent. T2DM patients meeting inclusion criteria were included. Patients were prescribed oral hypoglycemic agents and RAAS inhibitors as required. Measurements included serum creatinine, urinary albumin, urinary creatinine, and urinary haptoglobin. Statistical analysis compared uHCR with traditional biomarkers.

Results: uHCR demonstrated improved specificity over spot uHp and was comparable to uACR in predicting nephropathy in patients with both deranged and preserved renal function. uHCR persisted longer than uACR post-treatment, indicating its role in detecting residual renal dysfunction. Elevated uHCR in normoalbuminuric T2DM patients suggested its potential to predict nephropathy earlier than microalbuminuria.

Conclusion: Urinary haptoglobin and uHCR are promising tools for early detection and monitoring of DN. Preliminary findings suggest that uHCR could augment or replace uACR in predicting DN. Larger studies are needed to validate their predictive thresholds, refine accuracy, and assess confounding factors.

Keywords: Diabetic Nephropathy, Diabetic Kidney Disease, Haptoglobin, Urinary Biomarkers, Renal Dysfunction

INTRODUCTION

Diabetic nephropathy is the most common microvascular complication. It is also globally the leading cause of end-stage renal disease [1]. Diabetic Nephropathy affects 15-40% of type 1 and 5-20% of type 2 diabetic patients [2-10]. Microalbuminuria is the earliest clinically detectable stage of diabetic nephropathy at which appropriate interventions can retard, or reverse the progression of the disease [11]. However, multiple studies have shown that microalbuminuria is neither a sensitive nor a specific marker for development of diabetic nephropathy, especially in those with preserved renal function [12]. Between 38 % and 73% of patients with type 2 diabetes who develop CKD are normoalbuminuric, and it has come to be recognized that there is no correlation between microalbuminuria and renal lesions on biopsy [13,14]. Because of the variability of urine albumin and the recognition of so-called normoalbuminuric CKD, there has been an intensive search for other biomarkers for detecting early nephropathy.

Patients with type 2 diabetes with retained renal function [estimated glomerular filtration rate [eGFR > 60 mL/ min/ 1.73 m²] had a higher urinary haptoglobin [Hp] level than those with albuminuria, according to recent research conducted on people from the Veterans Affairs Diabetes Trial [15]. A similar study conducted by Jian Jun Liu et. al. [16] reported that there was an 11-fold increase in urinary haptoglobin level in patients with progressive decline in renal function [eGFR decline 3mL/min/1.73 m2/year] and that in the chronic kidney disease stage 3 subpopulation, urinary haptoglobin outperformed albuminuria for the prediction of rapid renal function decline. Haptoglobin is an acute phase plasma protein with hemoglobin-binding properties that primarily captures and eliminates free heme circulating in the blood and tissues. Haptoglobin is produced in the liver, lung, skin, spleen, kidney, and adipose tissue.

The purpose of this study is to assess whether urine haptoglobin, in the absence of albuminuria, can predict the onset of decline of renal function and to assess the diagnostic utility of urinary haptoglobin/creatinine [UHCR] ratio for early detection of diabetic nephropathy.

MATERIAL AND METHODS

A Prospective, analytical study was done of patients over 30 years of age with type 2 DM, visiting a tertiary care centre in Agra. Patients were selected on the basis of predefined inclusion and exclusion criteria. The Patients were divided based on their renal function into the following four groups: Group A - patients who have Diabetes Mellitus type 2 [T2DM] without Microalbuminuria (uACR <30mg/g) and normal GFR (eGFR >90ml/min/1.73 m2) [25], Group B - patients of T2DM with Microalbuminuria [uACR >30mg/g] and Normal GFR (eGFR >60ml/min/1.73 m2), Group C - T2DM patients with Albuminuria [uACR >30mg/g] and decreased GFR (eGFR < 60ml/min/1.73 m2), Group D - Control subjects who were Healthy, Non- Diabetic Volunteers not undergoing any treatment and willing to participate in the study had normal eGFR. Controls were taken from relatives or hospital staff after matching for average Age, Sex and BMI.

We investigated 193 patients, 48 were categorised into group A, 91 into Group B, and 54 into Group C. Patients of group B and C were also classified into 3 groups based on KDIGO classification of Albuminuria. We defined patients of T2DM who progressed into Diabetic Nephropathy by: (1) an annual eGFR decline of 3 mL/min per 1.73 m2 or greater, (2) Persistent albuminuria for more than 6 months despite therapy, (3) 6 months or more of follow-up without restoration to basal level [to exclude potential acute renal impairment], (4) Or an eGFR declining continuously during the follow-up period. We defined non-progressors as patients with eGFR change <2 mL/min per 1.73m2 per year despite 1 years or more of follow-up. The first study visit for all participants was the screening visit Repeat, followed by repeat visits were at 6th month and 12th month. A spot mid-stream urine sample was collected on patient's first visit which was voided directly into a sterile container. The sample was then aliquoted, centrifuged at 2000-3000 RPM and then stored at -20 °C. We avoided performing repeated freeze-thaw cycles. The samples were then later thawed and re-centrifuged for 20 minutes. The supernatant without sediment was then collected to run tests. Urinary haptoglobin was quantified by The BT Lab **Human Haptoglobin/Zonulin, HPT/HP ELISA Kit** [26], a sandwich type Enzyme-Linked Immunosorbent Assay [ELISA] performed with computer-based curve-fitting software on the ROBONIK readwell TOUCH ELISA plate reader and Urinary Haptoglobin: Creatinine ratio was calculated for each patient by dividing urinary Haptoglobin concentration in µg/dl by urinary creatinine concentration in g/dl. Statistical Analysis was done using IBM SPSS statistics tool 28.0.1.0. Differences in baseline clinical and biochemical variables between the 4 groups were compared by one way ANOVA test and Pearson coefficient was used to correlate relationships within data. Results were considered statistically significant when 'p value' was under 0.05.

RESULTS

The demographic and clinical characteristics of patients are shown in Table 1. The majority were male (56.4%), with a mean age of 52 ± 12 years. BMI averaged 23.91 ± 2.97 kg/m², and the mean HbA1c was 8.91 ± 1.99%. Retinopathy was observed in 15.5% of patients, while 22.7% were smokers. The mean eGFR was 82.99 ± 26.91 ml/min, reflecting varying renal function among the cohort.

Table 1 - Clinical and Biochemical Variables of sample population

Parameter	Value
Male	109 (56.4%)
Female	84 (43.6%)
Age (years)	52 ± 12
BMI (kg/m²)	23.91 ± 2.97
Duration of Illness (years)	5.96 ± 2.81
HbA1c (%)	8.91 ± 1.99
MAP (Male, mmHg)	90 ± 4
MAP (Female, mmHg)	86 ± 2
Retinopathy	30 (15.5%)
Smokers	44 (22.7%)
Total Cholesterol (mg/dl)	187 ± 54
eGFR (ml/min)	82.99 ± 26.91

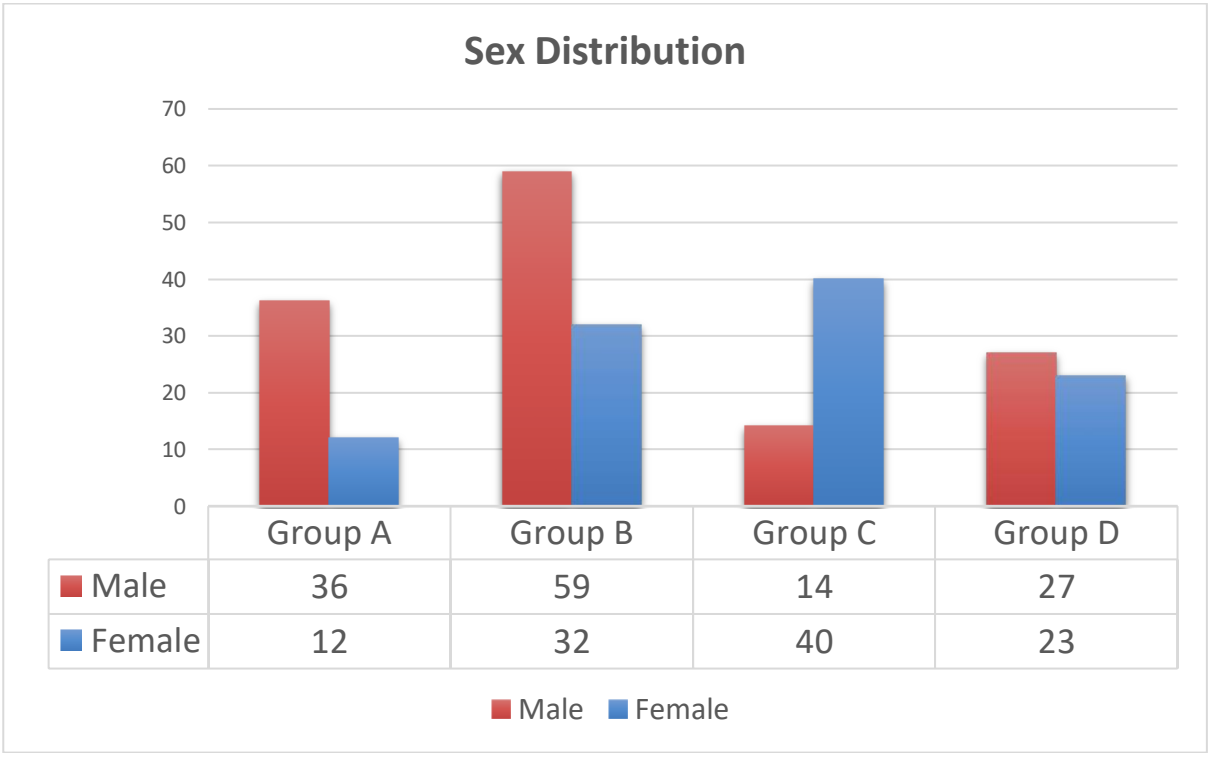

Figure 1 – Sex Distribution of Sample Population

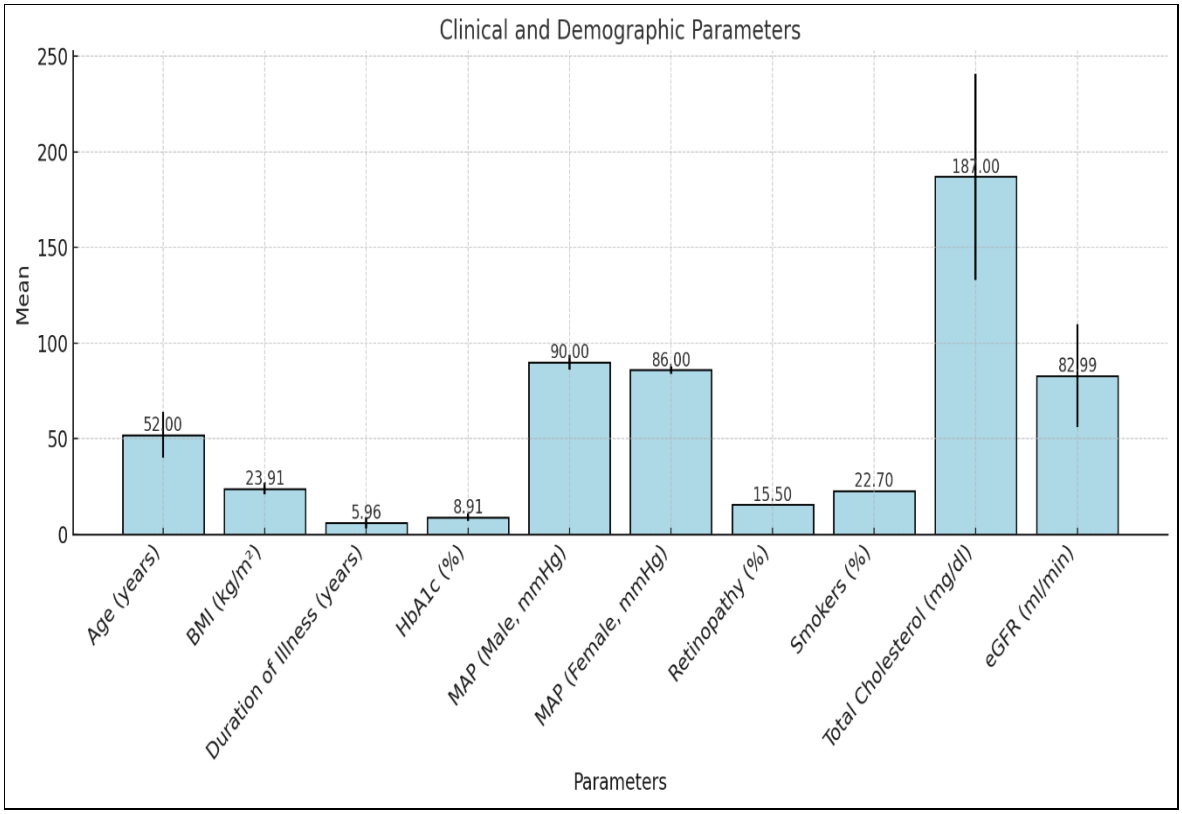

Figure 2 – Clinical and Demographic Parameters

An age-based distribution of participants across four groups (A, B, C, and D) is shown in Table 2. Group A shows the highest proportion (50%) in the 40-60 age range, with 33.33% being under 40 and 16.67% above 60. Group B is predominantly in the 40-60 age range (64.84%), followed by 21.98% above 60 and 13.19% under 40. In Group C, most participants (51.85%) are above 60, with 44.44% aged 40-60 and only 3.70% under 40. Group D also has a majority in the 40-60 range (52%), with 26% above 60 and 22% under 40. This data highlights the varying age demographics across the groups, with a notable prevalence of middle-aged participants in Groups A, B, and D, while Group C skews older.

Table 2 - Age-related distribution of each group of samples

Age group [yrs.]	Group A		Group B		Group C		Group D	
	No.	%	No.	%	No.	%	No.	%
<40	16	33.33	12	13.19	2	3.70	11	22.00
40-60	24	50.00	59	64.84	24	44.44	26	52.00
>60	8	16.67	20	21.98	28	51.85	13	26.00
Total	48	100.00	91	100.00	54	100.00	50	100.00

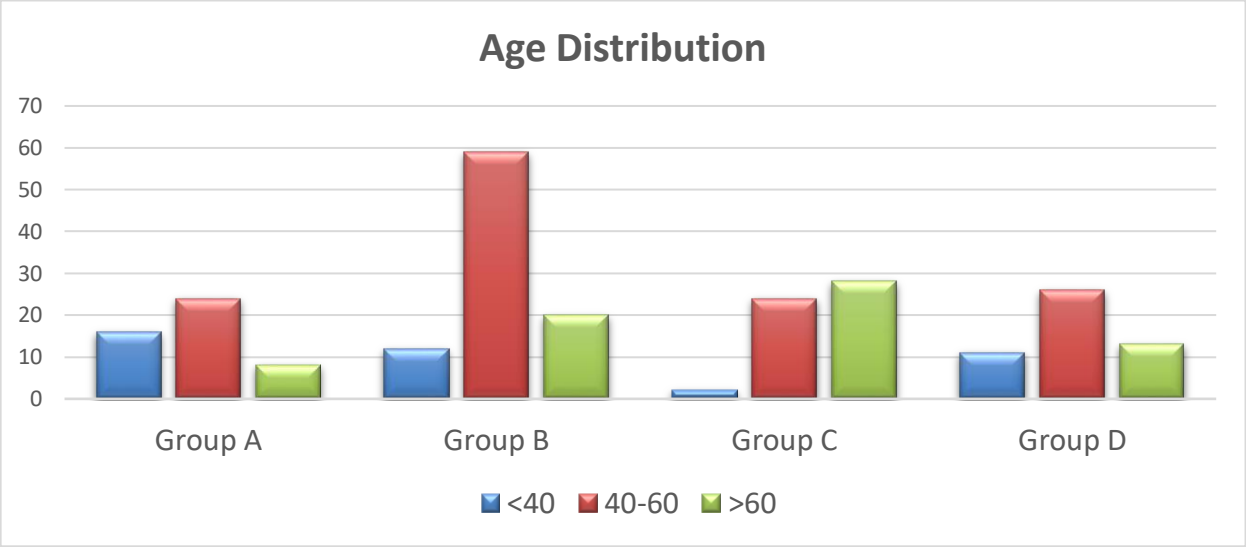

Figure 3- Age-related distribution of each group of samples

The eGFR distribution across groups is shown in Table 3. It is showing significant differences ($p < 0.0001$). Group D (control) had the highest mean eGFR (119.87 ± 4.8 ml/min), followed by Group A (100.92 ± 20.68 ml/min) and Group B (93.45 ± 17.71 ml/min). Group C had the lowest eGFR (49.15 ± 8.33 ml/min), indicating severe renal impairment. These results emphasize the progression of renal dysfunction across groups.

Table 3 – eGFR of Sample Population

Group	Frequency	eGFR		p-value	f-value	CD at 5%
		Mean	SD			
A	48	100.92	20.68	<0.0001	211.021	7.46
B	91	93.45	17.71			
C	54	49.15	8.33			
D (Control)	50	119.87	4.8			

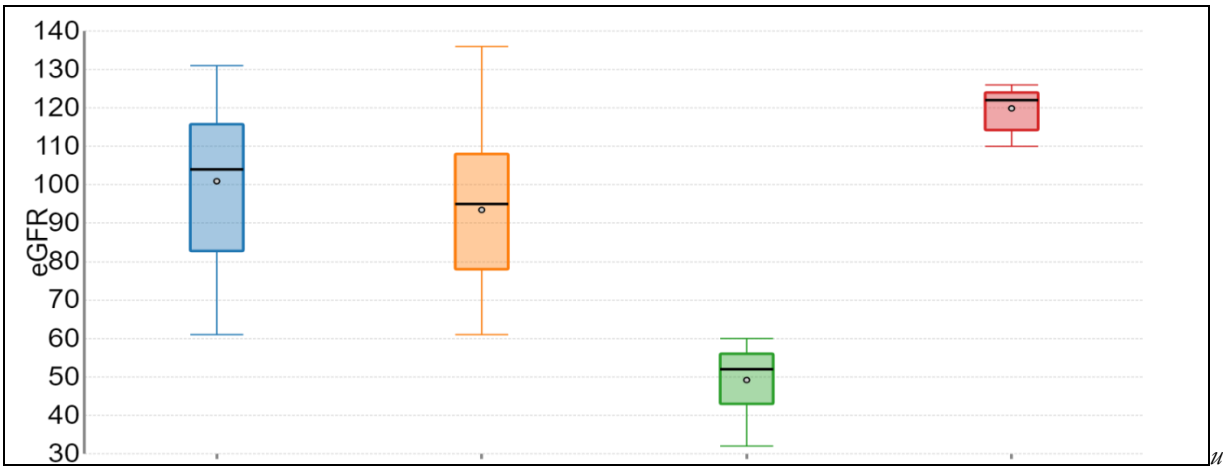

Fig re 4- eGFR of Sample Population

KDIGO eGFR stages across Groups A, B, and C are shown in Table 4. In the G1 category (eGFR >90), the majority were from Group A (32) and Group B (53), totaling 85 participants. The G2 category (eGFR 60-89) included 16 participants from Group A and 38 from Group B, totaling 54. Groups C exclusively represented G3 stages, with 38 participants in G3a (eGFR 45-59) and 16 in G3b (eGFR 30-44). This distribution highlights that Groups A and B predominantly maintain higher eGFR levels, while Group C experiences advanced renal dysfunction.

Table 4 – CKD Classification of Sample Population

KDIGO Category	eGFR	Group A	Group B	Group C	Total
G1	>90	32	53		85
G2	60-89	16	38		54
G3a	45-59			38	38
G3b	30-44			16	16

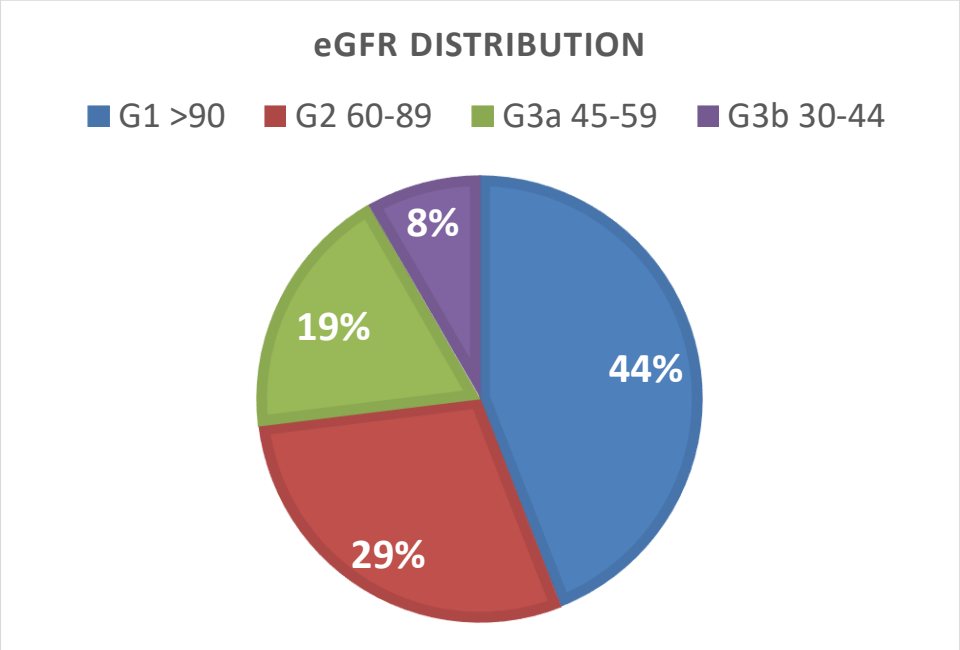

Figure 5 – eGFR distribution of sample population

Urinary microalbumin levels across four groups are shown in Table 5. Group C showed the highest mean microalbumin levels (38.75 ± 13.79 mg/dl), followed by Group B (15.28 ± 8.75 mg/dl) and Group A (4.39 ± 4.02 mg/dl). Group D had the lowest levels (1.08 ± 0.39 mg/dl), indicating minimal renal impairment. Statistical analysis revealed a highly significant difference between the groups ($p < 0.0001$, f-value = 20.510), with a critical difference (CD) of 13.60 at 5%.

Table 5 – Spot urinary albumin of sample population

Urinary microalbumin (mg/dl)						
Group	**Frequency**	**Mean**	**SD**	**p-value**	**f-value**	**CD at 5%**
A	48	4.39	4.02	<0.0001	20.510	13.60
B	91	15.28	8.75			
C	54	38.75	13.79			
D	50	1.08	0.39			

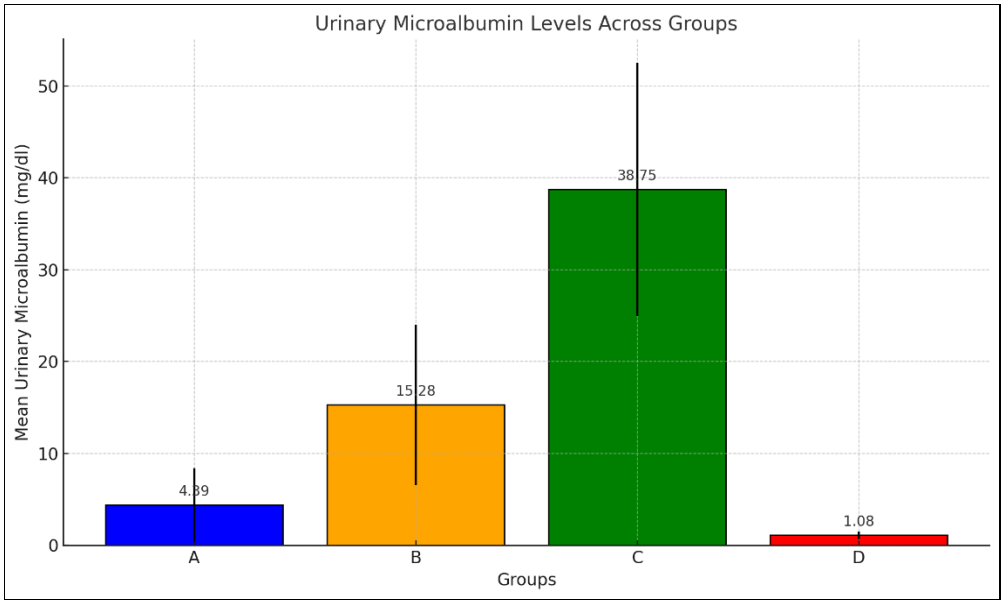

Figure 6- Urinary Microalbumin Levels Across Groups

Spot urinary haptoglobin levels across groups are shown in Table 6. Group C had the highest levels (108.08 ± 26.84 µg/ml), followed by Group B (89.80 ± 26.32 µg/ml) and Group A (70.77 ± 27.83 µg/ml). Group D (control) had the lowest levels (39.84 ± 21.30 µg/ml). The differences were statistically significant ($p < 0.0001$), indicating a correlation between increasing urinary haptoglobin levels and worsening renal function.

Table 6 – Spot Urinary Haptoglobin of the Sample population

Group	Frequency (No. of patients)	Urinary Haptoglobin (µg/ml)		p-value	f-value	CD at 5%
		Mean	SD			
A	48	70.77	27.83	<0.0001	9.8373	12.90
B	91	89.80	26.32			
C	54	108.08	26.84			
D (Control)	50	39.84	21.30			

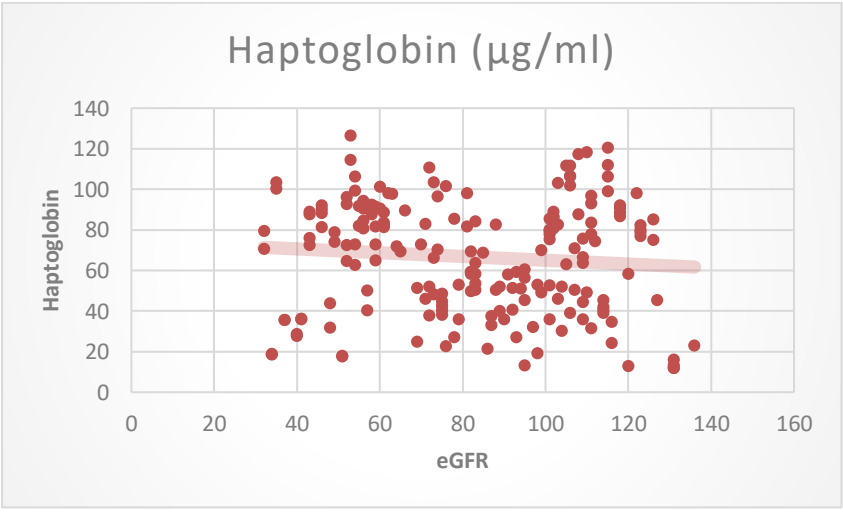

Figure 7 – Scatter Diagram of Urinary Haptoglobin of sample population

Urinary albumin-to-creatinine ratio (uACR) and Urinary haptoglobin-to-creatinine ratio (uHCR) across groups are shown in Table 7. Group C had the highest mean values for both uACR (350.05 ± 265.75 mg/g) and uHCR (260.54 ± 192.64 µg/g), followed by Group B (uACR: 184.12 ± 123.85 mg/g; uHCR: 117.74 ± 116.29 µg/g) and Group A (uACR: 19.26 ± 7.23 mg/g; uHCR: 47.32 ± 34.92 µg/g). Group D (control) showed the lowest values (uACR: 6.46 ± 2.5 mg/g; uHCR: 5.16 ± 2.22 µg/g). The differences in both uACR and uHCR across groups were statistically significant ($p < 0.0001$), with f-values of 90.275 and 42.85, respectively.

Table 7 – Correlation between uACR and uHCR

Group	Frequency	uACR(mg/g)		uHCR (µg/g)	
		Mean	SD	Mean	SD
A	48	19.26	7.23	47.32	34.92
B	91	184.12	123.85	117.74	116.29
C	54	350.05	265.75	260.54	192.64
D (Control)	50	6.46	2.5	5.16	2.22
f-value	90.275			42.85	
p-value	<0.0001			<0.0001	
CD at 5%	218.11			601.22	

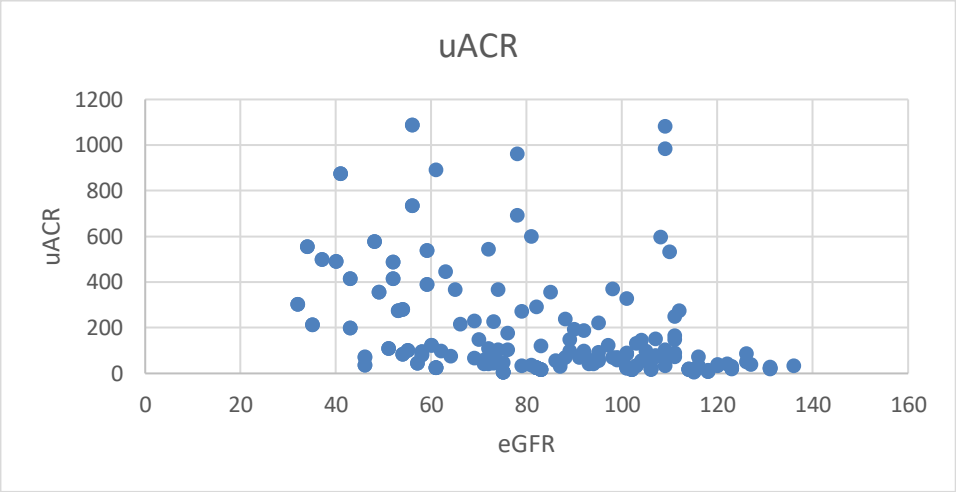

Figure 8 – Scatter Diagram of uACR of sample population as a whole

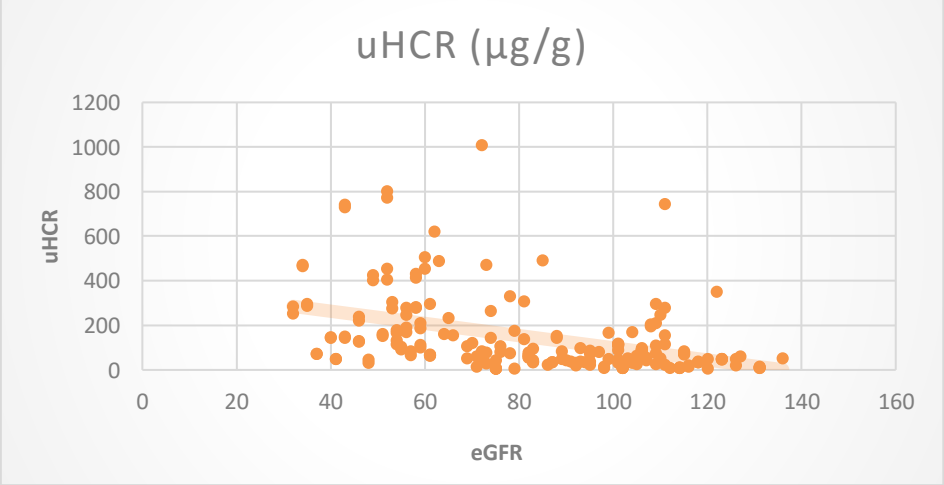

Figure 9 – Scatter diagram of uHCR of Sample population

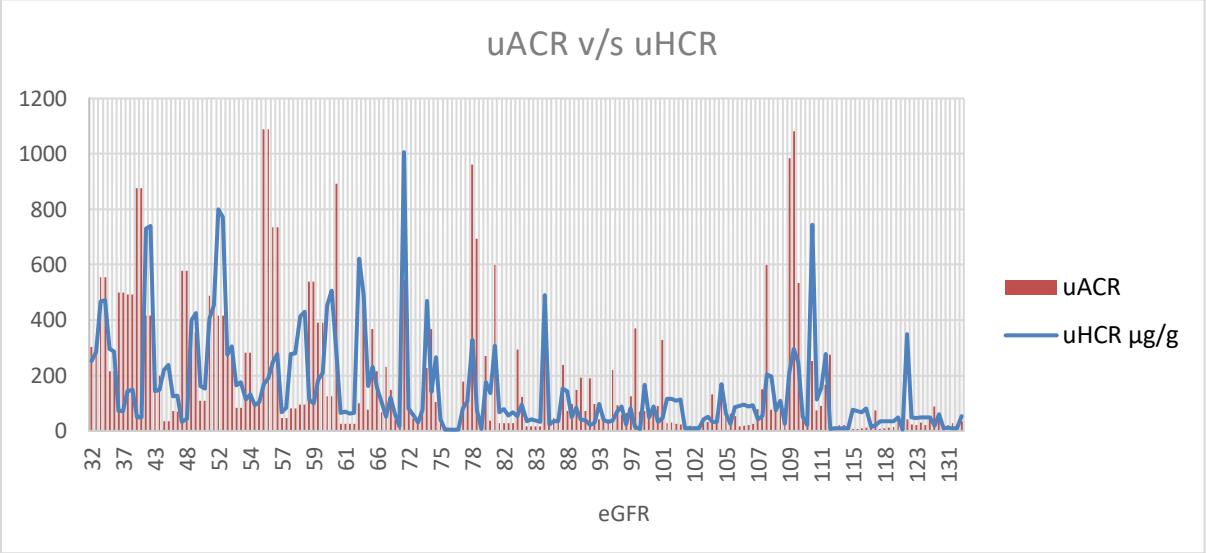

Figure 10– uACR v/s uHCR

uHCR levels with eGFR categories is shown in Table 8. In early stages (G1 and G2), most patients had uHCR <80 µg/g, while advanced stages (G3a and G3b) showed a higher proportion with uHCR >80 µg/g. Specifically, G3a had 33 patients with elevated uHCR, and G3b had 12. This trend highlights the correlation between worsening eGFR and higher uHCR levels, reinforcing its potential as a marker for renal dysfunction.

Table 8 – uHCR v/s eGFR in Sample population at Baseline

KDIGO Category	eGFR	Number of Patients	Patients with uACR >30 mg/dl	Patients with uHCR >80 µg/g	Patients with uHCR <80 µg/g
G1	>90	85	54	27	58
G2	60-89	54	40	26	28
G3a	45-59	38	36	33	5
G3b	30-44	16	16	12	4

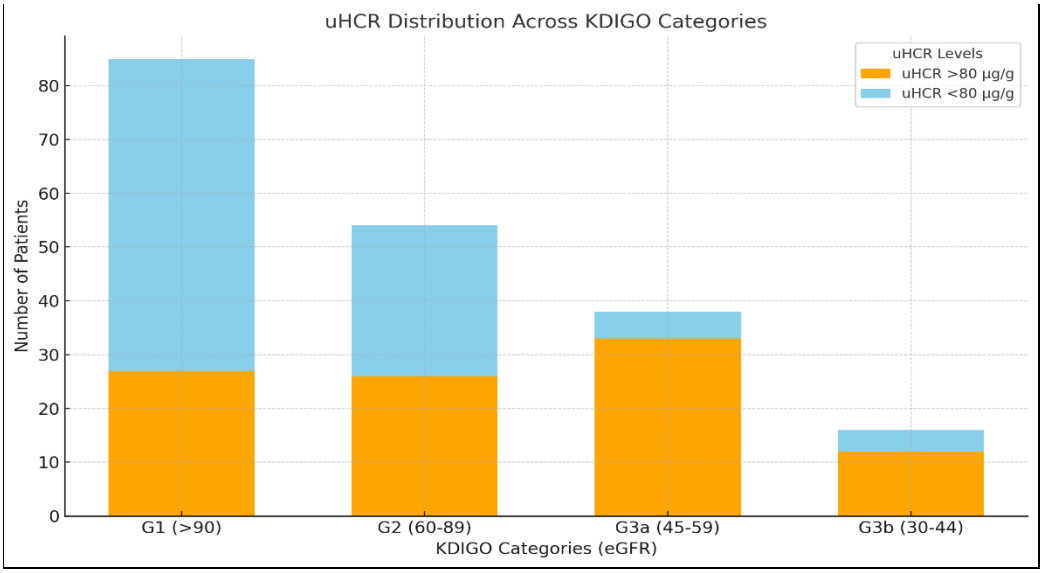

Figure 11 – uHCR Distribution Across KDIGO Categories (eGFR)

uHCR (>80 µg/g) distribution across uACR categories at baseline is shown in Table 9. In Group A, 9 patients with uACR <30 mg/g had elevated uHCR levels. For uACR 30-300 mg/g, 30 and 25 patients in Groups B and C, respectively, had uHCR >80 µg/g. In the >300 mg/g category, 12 patients in Group B and 22 in Group C showed elevated uHCR. This trend suggests a correlation between higher uACR levels and elevated uHCR, particularly in Groups B and C.

Table 9 – uHCR v/s uACR in Sample population at Baseline

	Group A		Group B		Group C	
	Frequency	Patients with uHCR >80 µg/g	Frequency	Patients with uHCR >80 µg/g	Frequency	Patients with uHCR >80 µg/g
	48	9	-	-	-	-

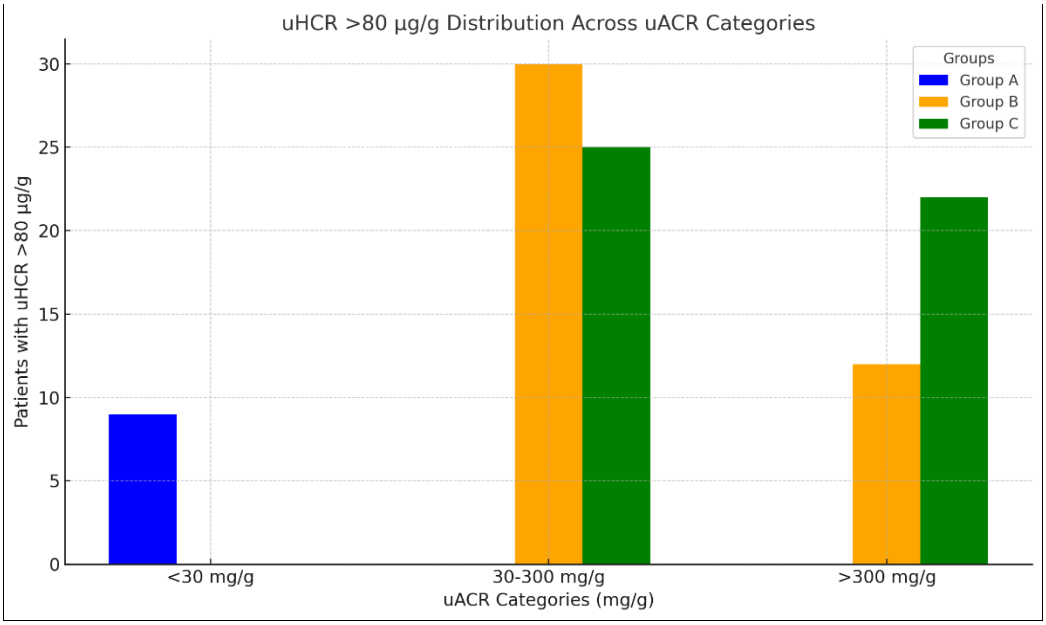

Figure 12 – uHCR >80 µg/g Distribution Across uACR Categories

The follow-up data for patients across three groups at 6 and 12 months is shown in Table 10. In Group A, 26 patients were followed up at 6 months, increasing to 33 at 12 months, with 15 patients lost to follow-up. Group B had 81 patients at 6 months and 70 at 12 months, with 21 patients lost to follow-up. Group C showed consistent follow-up rates, with 48 at 6 months and 50 at 12 months, losing only 4 patients.

Table 10 – No. of Patients at Follow-up visits

Sample Groups	Total No. of Patients	6 months	12 months	Total Patients lost to Follow-Up
GROUP A	48	26	33	15
GROUP B	91	81	70	21
GROUP C	54	48	50	4

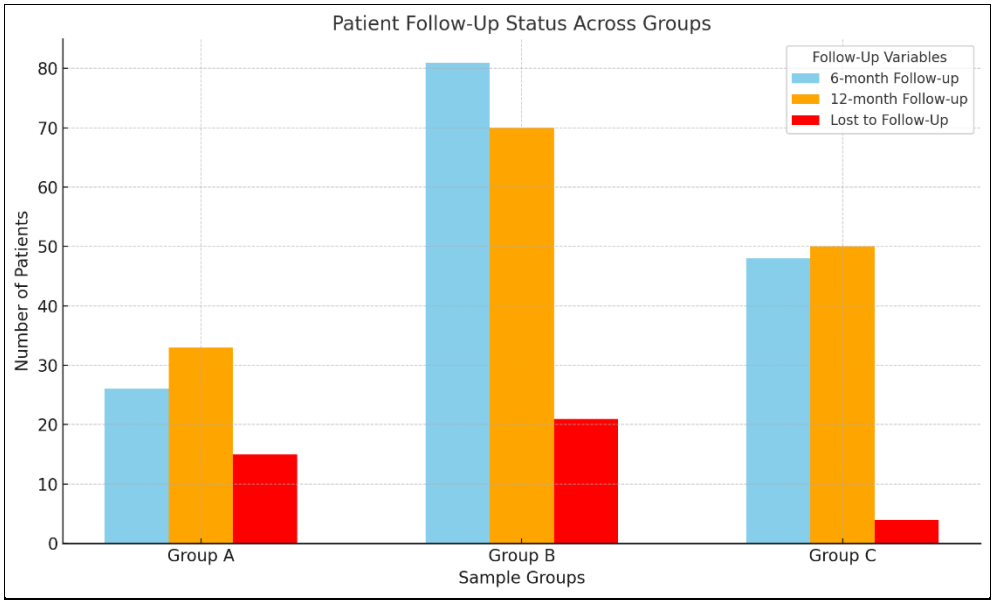

Figure 13 – Patient Follow up status across groups

The trends in uACR, urinary haptoglobin, and uHCR across three groups over a 1-year follow-up are shown in Table 11. Group C consistently had the highest baseline values for uACR (350.05 ± 265.75 mg/g), urinary haptoglobin (108.08 ± 26.84 µg/ml), and uHCR (260.55 ± 192.64 µg/g), which significantly reduced to 48.36 ± 29.87 mg/g, 33.45 ± 29.43 µg/ml, and 139.93 ± 100.55 µg/g, respectively, by 12 months. Group B showed similar improvements, with uACR declining from 184.12 ± 123.85 mg/g to 34.86 ± 8.13 mg/g, urinary haptoglobin from 89.80 ± 26.32 µg/ml to 27.28 ± 22.36 µg/ml, and uHCR from 117.74 ± 116.29 µg/g to 70.89 ± 55.27 µg/g. Group A maintained relatively lower values throughout, with minor fluctuations and a slight decrease at 12 months (uACR: 18.41 ± 6.36 mg/g, urinary haptoglobin: 34.26 ± 10.3 µg/ml, uHCR: 21.03 ± 16.43 µg/g). These trends indicate a progressive reduction in renal stress markers over time, particularly in Groups B and C, demonstrating the impact of therapy and disease progression control.

Table 11 – uACR (mg/g), Urinary Haptoglobin (µg/ml) and uHCR (µg/g) trend over 1 year

Sample Groups	**Total No. of Patients**	**1ST VISIT**		**6 month**		**12 month**	
		MEAN	**SD**	**MEAN**	**SD**	**MEAN**	**SD**
uACR (mg/g)							
GROUP A	33	19.26	7.23	**20.67**	**6.75**	**18.41**	**6.36**
GROUP B	70	184.12	123.85	**75.37**	**14.03**	**34.86**	**8.13**
GROUP C	50	350.05	265.75	**120.20**	**104.67**	**48.36**	**29.87**
Urinary Haptoglobin (µg/ml)							
GROUP A	33	70.77	27.83	**54.35**	**24.02**	**34.26**	**10.3**
GROUP B	70	89.80	26.32	**40.08**	**26.48**	**27.28**	**22.36**
GROUP C	50	108.08	26.84	**49.71**	**29.18**	**33.45**	**29.43**
uHCR (µg/g)							
GROUP A	33	47.32	34.92	**40.15**	**28.14**	**21.03**	**16.43**
GROUP B	70	117.74	116.29	**94.272**	**65.97**	**70.89**	**55.27**
GROUP C	50	260.548	192.64	**199.032**	**132.137**	**139.934**	**100.55**

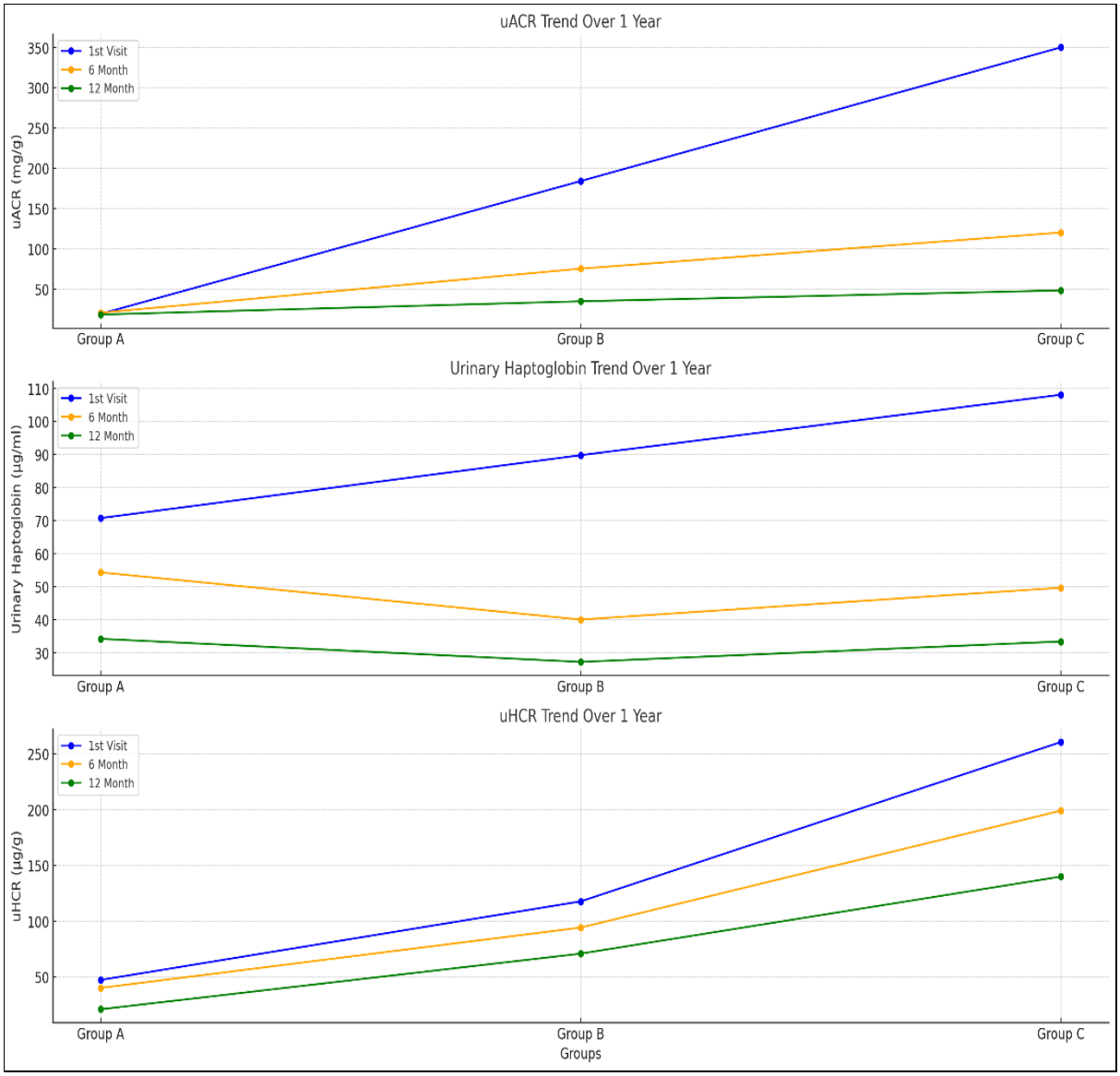

Figure 14 - The trends in uACR, urinary haptoglobin, and uHCR across three groups over a 1-year follow-up

The number of patients who progressed to diabetic nephropathy across the groups are shown in Table 12. Group C had the highest number of progressors (28), with nearly half of its patients progressing, while 22 remained non-progressors. Group B had 17 progressors and 53 non-progressors, indicating better disease control compared to Group C. Group A showed the least progression, with only 2 patients progressing and 31 remaining non-progressors

Table 12 – No. of patients that progressed to Diabetic Nephropathy

Sample Groups	Total No. of Patients	PROGRESSORS	NON-PROGRESSORS
GROUP A	33	2	31
GROUP B	70	17	53
GROUP C	50	28	22

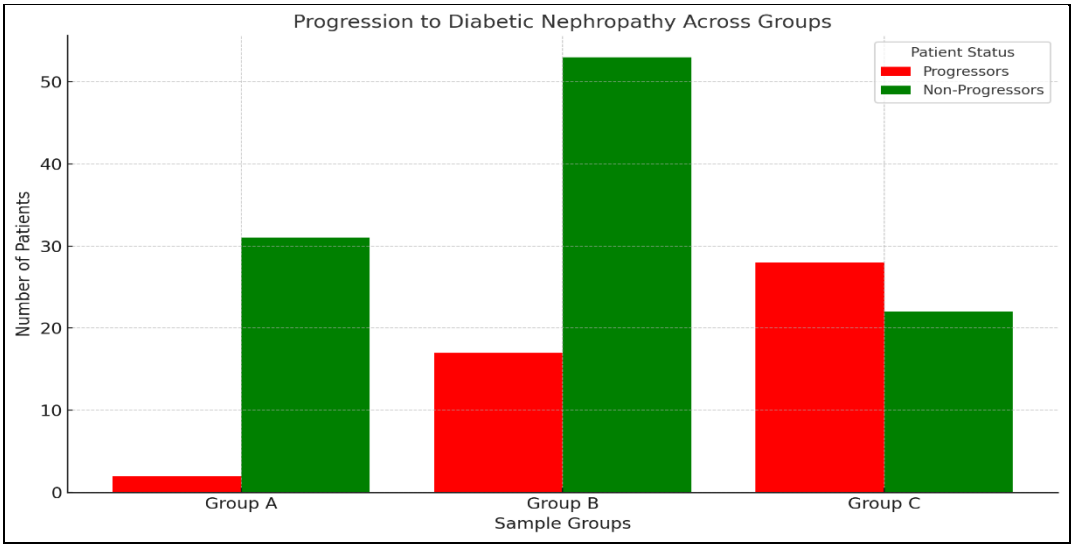

Figure 15 - No. of patients that progressed to Diabetic Nephropathy

The progression to diabetic nephropathy based on urinary haptoglobin levels across three groups is shown in Table 13. In Group A, 28 patients had urinary haptoglobin >70 µg/ml, with only 2 progressors, while none of the 5 patients with haptoglobin <70 µg/ml progressed. Group B had 35 patients with haptoglobin >70 µg/ml, of whom 17 progressed, while none of the 35 patients with levels <70 µg/ml progressed. Group C had the highest progression rate, with 22 of 39 patients with haptoglobin >70 µg/ml progressing, and 6 of 11 patients with haptoglobin <70 µg/ml also showing progression.

Table 13 – Progressors on basis of Urinary Haptoglobin Value

Sample Groups	Total No. of Patients	Urinary Haptoglobin > 70 µg/ml		Urinary Haptoglobin < 70 µg/ml	
		Frequency	No. of Progressors	Frequency	No. of Progressors
Group A	33	28	2	5	0
Group B	70	35	17	35	0
Group C	50	39	22	11	6

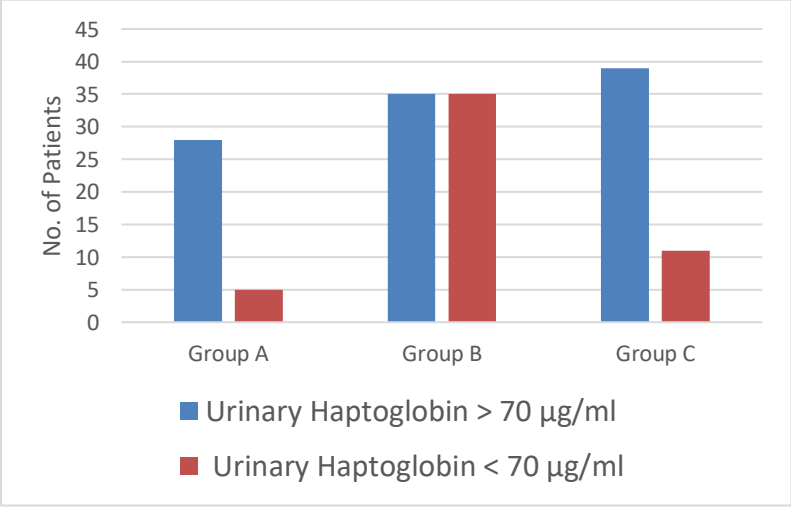

Figure 16 – Population split with Urinary Haptoglobin 70 µg/ml as median

Progression to diabetic nephropathy based on uHCR levels across groups is shown in Table 14. In Group A, 9 patients had uHCR >80 µg/g, with 2 progressing, while none of the 24 patients with uHCR <80 µg/g progressed. In Group B, 42 patients had uHCR >80 µg/g, with 17 progressing, while none of the 28 patients with uHCR <80 µg/g progressed. Group C had the highest progression rate, with 28 of 47 patients with uHCR >80 µg/g progressing, and none of the 3 patients with uHCR <80 µg/g progressing.

Table 14 - Progressors on basis of uHCR Value

	Total No. of Patients	uHCR > 80 µg/g		uHCR < 80 µg/g	
		Frequency	No. of Progressors	Frequency	No. of Progressors
Group A	33	9	2	24	0
Group B	70	42	17	28	0
Group C	50	47	28	3	0

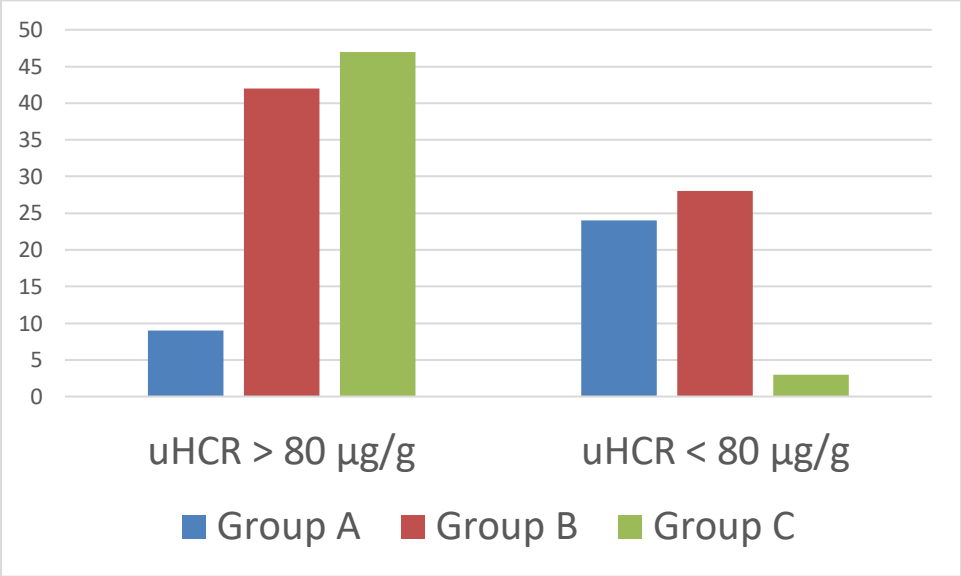

Figure 17 - Population split with uHCR 80 µg/g as median

DISCUSSION

Urinary haptoglobin is proteomic biomarker and currently being used for evaluating the early detection diabetic nephropathy before the onset of microalbuminuria [17][18][19]. Various studies in member of different cohorts suggest that early intervention may delay and prevent the onset of microalbuminuria and unwanted adverse events associated with diabetic nephropathy. Efforts are being made to predict about progression to ESRD in patients with persistent microalbuminuria. our study also made one step forward in this direction.

The cohort included in this work had varying levels of albuminuria ranging from normoalbuminuric patients to different stages of diabetic nephropathy. In our study, urinary haptoglobin predicted early renal function decline in a Group A (T2DM patient without microalbuminuria and preserved renal function in two patients) while in group B 17 patients of T2DM shift microalbuminuria and preserved renal function at baseline progressed to diabetic nephropathy.[20] These subset of patients had urinary haptoglobin above the median value of 70 mcg/ml while rest of 53 Patient in this group improved and became normoalbuminuric at the end of 1 year with control of diabetes mellitus and RAAS therapy and urinary haptoglobin also decrease. In Group C, 28 patients out of the 50 with higher level of urinary haptoglobin had further decline in renal function on while 22 patients improved at the end of 1 year with control of DM had lower the level of urinary haptoglobin (<70 mcg/ml). these reports are similar to earlier study by Bhensdadia NM et. al. [15]. Thus, we can conclude that urinary haptoglobin is good predictor of risk of progression to diabetic nephropathy. Yang et.al. [21] also demonstrated that urinary haptoglobin can predict the

early renal function decline in T2DM patient with CKD stage 1,2 and 3. Jian-jun liu et. al. [16] also observed that urinary haptoglobin can predict rapid renal function decline in Asian with T2DM with early kidney disease. In Indian population Bhensdadia NM et. al. [15] also demonstrated the similar observation.

In our study, the median for urinary haptoglobin at baseline was found to be 70.84 µg/ml, the change in values can be attributed to a difference in Test-Kits or difference in population. Patients were segregated on the basis of values higher or lower than 70 µg/ml at baseline, where patients with urinary Haptoglobin levels > 70 µg/ml were considered to be at high risk of progression to nephropathy. According to study by Bhensdadia NM et. al. urinary Haptoglobin levels had a mean of 158 ng/ml and median was 70 ng/ml and patients were then segregated into 2 groups, based on the median value [15].

We also observe that uHCR has better specificity of spot urinary haptoglobin and comparable to uACR in predicting nephropathy in T2DM patients. similar finding were observed by Bhensdadia NM et. al.[15]. However we also found that UHCR resolved later in patients as compared to uACR. This indicate that renal dysfunction persist even after return to normoalbuminuric state after the therapy. this is our observation that T2DM patients with normal albuminuria and uACR had deranged uHCR value. this suggest that uHCR like urinary haptoglobin may be superior to UACR in early detection and progression of nephropathy before the onset of microalbuminuria.
Haptoglobin is circulating protein and potent angiogenic factor in neovascular development [22].It stimulate the tissue repair and colleterals vessels growth in an inflammatory milleu as compensation to ischemic injury. increase urinary haptoglobin secretion may indicate ongoing tissue injury, repair and microvascular remodelling, which predicts high risk for rapid renal function decline. Our preliminary study suggests that urinary haptoglobin may be first biomarker to augment or replace UACR in early prediction and detection of progression of diabetic nephropathy.

CONCLUSION

Our study demonstrated that urinary haptoglobin is reliable marker for early detection and progression of diabetic nephropathy. thus, urine haptoglobin could be potential diagnostic tool in early identification of diabetic nephropathy.

LIMITATIONS OF THE STUDY

In our study, we were primarily limited by the duration of the study. T2DM in itself is usually detected late in the course of the disease. A period of 1 year is not sufficient to detect progression of patients to diabetic nephropathy. We diagnosed patients as having diabetic nephropathy on the basis of spot uACR and deranged eGFR and the persistence of these derangements throughout the course of the study.

Further follow-up and monitoring of the patients in this study is needed for precise evaluation and prediction of progression to DN.

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Tables/Figures **– (<6 combined)**
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