Pro Index Journal of Science in Medicine and Life
Volume: 2 Issue: 3 Year: 2024
http://journals.proindex.uz

A Comparison between Beta Trace Protein, Cystatin C and Creatinine for the Estimation of eGFR in Diabetic Nephropathy

Kamal AL-Deen Hussein Ali
Department of Chemistry, Faculty of Science, University of Çankiri Karatekin, Turky

Aya Yassin Taher
Department of Biology, College of Science, Al-Ameen University, Baghdad, Iraq

Abstarct: **BACKGROUND:** Diabetes mellitus type 2 is considered the main source of diabetic nephropathy, as the proportion of patients who developed diabetic nephropathy is approximately 45% as a result of type 2 diabetes. It is also considered a cause of kidney patients at the end of the stage. Glomerular filtration rate (GFR) is the best functional parameter for renal diseases.

AIM: The aimed of this study was to determine in comparison between Beta Trace Protein, cystatin C and creatinine for the estimation of eGFR in type 2 Diabetic Nephropathy.

MATERIALS AND METHODS: A Case-control study included of 120 Persons with T2DM of both gender (40-69 years, 64 males and 56 females), divided into four groups: Group I: includes 30 persons as a healthy control (UACR < 30 mg/g creatinine). Group II: includes 30 patients with type2 DM normoalbuminuria (UACR < 30 mg/g creatinine) as a control. Group III: includes 30 patients with type 2 DM microalbuminuria (UACR 30 – 300 mg/g creatinine). Group IV: includes 30 patients with type 2 DM macroalbuminuria (UACR > 300 mg/g creatinine).

RESULTS: the level of GFR βTP is marked decrease than GFR Cystatin C and GFR Cr. in early stage microalbuminuria cumbered with normoalbuminuria group , the results of the current study showed an inverse correlation between BTP and GFR BTP in healthy control group, normalbumin group, microalbumin group and macroalbumin group and a positive correlation between Cystatein C and GFR BTP in normalbumin group, inverse correlation between Cystatein C and GFR Cys.c in healthy control group, normalbumin group, microalbumin group and macroalbumin group and a positive correlation between GFR Cr and GFR Cys.c and GFR BTP in healthy control group, a positive correlation between GFR Cr and GFR Cys.c in normalbumin group and a positive correlation between GFR Cr and GFR BTP in macroalbumin group.

CONCLUSION: the level of GFR βTP is better than GFR Cystatin C and GFR Cr. which may be considered as a predictive marker for the estimation of eGFR in type 2 Diabetic Nephropathy.

Key points: Beta Trace Protein, eGFR BTP, Type2-diabetes mellitus, Diabetic Nephropathy.

Introduction:

Diabetic nephropathy is a clinical syndrome it is defined by proteinuria > 500 mg in 24 hours in the setting of diabetes, but this is preceded by lower degrees of proteinuria, or "microalbuminuria Diabetic nephropathy, also known as Kimmelstiel Wilson syndrome or nodular diabetic glomerulosclerosis or intracapillary glomerulonephritis [1]. **Beta Trace Protein (BTP)** is a novel endogenous marker of glomerular filtration rate (GFR). It was initially reported in 1961, and in 1997 it was discovered to be elevated in the serum of individuals with renal illness [2]. According to the degree of glycosylation, beta trace protein (βTP), also known as lipocalin-type prostaglandin D2 synthase (LPGDS), is a monomeric glycoprotein with 168 amino acids and a low molecular weight

(23-29 KD) [3]. **Cystatin C** is a low-molecular weight protein, is produced by all nucleated cells at a constant rate, unaffected by such factors as muscle mass and diet [4]. It is directly and freely filtered through the glomerulus with complete tubular reabsorption and catabolization, no reabsorption into the bloodstream, and no renal tubular secretion. As such, Cys C is regarded as a good filtration marker [5]. **Glomerular Filtration Rate (GFR)** is a primary parameter to check the kidney function, and it shows the plasma flow from the glomerulus into Bowman's space over a particular period [6]. The classic and popular method for evaluating kidney function and determining the stage of renal disease is GFR measurement [7]. This study aimed to determine in comparison between Beta Trace Protein, cystatin C and creatinine for the estimation of eGFR in type 2 Diabetic Nephropathy.

Materials and Methods

A Case- control studies included of 120 Persons (30 person healthy control and 90 patients proved with T2DM of both gender (40-69 year, 64 males and 56 females), divided into four groups shown below. Collected during the period between January 2022 and September 2022, the permission to do the research was obtained for out-patients by the consultation unit of diabetes consultant in Salah El-din Hospital / Salah El-din Governorate. Patient's criteria for inclusion: Iraqi patients with T2DM at duration more than 5 years of the occurrence of diabetes. Patient criteria for exclusion: Excluded patients with CVD, Duration of type 2 DM less than 5 years, pregnancy, acute infections.

The study groups A total sample of study be 120, there are 90 samples of patients Type 2 Diabetes Mellitus (T2DM) at duration 5-19 years of the diagnosis of diabetes was divided into four groups by using proteinuria and Urinary Albumin to Creatinine Ratio (UACR) as following: **Group I:** includes 30 persons as a healthy control (UACR < 30 mg/g creatinine). **Group II:** includes 30 patients with type2 DM normoalbuminuria (UACR < 30 mg/g creatinine) as a control. **Group III:** includes 30 patients with type 2 DM microalbuminuria (UACR 30 – 300 mg/g creatinine). **Group IV:** includes 30 patients with type 2 DM macroalbuminuria (UACR > 300 mg/g creatinine).

Estimation of GFR By using the formulary of chronic kidney diseased epidemiological collaboration (CKD-EPI).

Table (1): CKD-EPI equations for eGFRCr, eGFR Cystatin C and eGFRβTP.

Equations
CKD-EPI equations for eGFRCr. **[8].**
$eGFRCr = 141 \times \min(S.Cr/\kappa, 1)^{\alpha} \times \max(S.Cr/\kappa, 1)^{-1.209} \times 0.993^{age}$ (× 1.018 if female) (× 1.159 if black)
Abbreviations / Units: Scr = standardized serum creatinine in mg/dL; divide by 88.4, for creatinine in μmol/L, κ = 0.7 (females) or 0.9 (males), α = -0.241 (female) or -0.302 (male), min(Scr/κ, 1) is the minimum of Scr/κ or 1.0, max(Scr/κ, 1) is the maximum of Scr/κ or 1.0, age (years)
CKD-EPI equations for eGFR Cystatin C. **[8].**
$eGFRCys.C = 133 \times \min(Scys/0.8, 1)^{-0.499} \times \max(Scys/0.8, 1)^{-1.328} \times 0.996^{age}$ (× 0.932 if female)
CKD-EPI developed equations for eGFRβTP. **[9].**
$eGFR\beta TP = 55 \times \beta TP^{-0.695} \times 0.998^{age}$ (× 0.899 if female)

About (5 – 7 ml) of blood samples were taken from healthy persons and patients having T2DM. each blood samples divided into two parts:

A) The first part of whole blood retained in Ethylenediaminetetraacetic acid (EDTA) tubes for measuring HbA1c by Cobas C311.

B) The second part of blood were left for 30 min at room temperature allows samples to clot in plain tube. After coagulation, Seram were separated by centrifugation at 3000 rpm for 10 min. Seram were aspirated and divided into two aliquots in Eppendorf tubes for: Aliquot 1: measurements of Seram Creatinine, Seram Urea, Seram Cholesterol, Seram Triglycerides and High-density lipoprotein the assay was applied by automated method by using Cobas C311. Aliquot 2: The rest were stored at (< -35 C°) until assayed for Serum Beta Trace Protein (BTP). Was measured using enzyme-linked immunosorbent assay (ELISA) by device HumaReader HS.

Five to ten milliliters (ml) of freshly collected morning urine samples were placed in a clean, dry container. Utilizing the Dimension EXL 200 integrated chemistry system evaluated basic urine testing that covers Urine Albumin/Creatinine Ratio, Microalbumin, and Protein.

Statistical analysis: Data of patients were analyzed using SPSS version 26.0 software. Descriptive statistics were tabulated as mean, stander deviation and stander error. ANOVA test was used to evaluate the difference in mean level of numeric data, Chi-square test used to test association between qualitative variables. Pearson correlation regression r was used to evaluate correlation between Numeric data, when r < 0.2 indicate week correlation, 0.2-0.8 indicate moderate correlation, > 0.8 indicate strong correlation. Scattered dot diagrams were used to show correlation between the variables. p value was <0.05 considered significance.

Results

Patients and healthy control: included 120 subjects from both sexes (female and male), which is divided into four groups according to their urinary albumin to creatinine ratio (UACR). showed the clinical characteristics of the four study groups significant difference as shown in the table (2 and 3).

Table (2): Anthropometry of Clinical characteristic, about investigation parameters in all studied groups, were shown as follows:

Clinical Variables		Group I (n=30) Non diabetics (Control)	Diabetics (N=90)			P-value*
			Group II (n=30) (Normoalbuminuria)	Group III (n=30) (Microalbuminuria)	Group IV (n=30) (Macroalbuminuria)	
Gender	Female	14	13	15	14	56
	Male	16	17	15	16	64
Age (years)	M±SD	51.133 ± 8.215	52.166 ± 8.034	54.766 ± 8.736	55.333 ± 5.797	0.001
	SE	1.499	1.466	1.595	1.058	
BMI (Kg/m2)	M±SD	25.154 ± 2.344	27.010 ± 2.775	28.300 ± 2.641	28.027 ± 4.024	0.001
	SE	0.427	0.506	0.482	0.734	
Duratio Diabetic	M±SD	-	5.700 ± 0.836	8.266 ± 1.048	12.733 ± 2.958	0.001
	SE	-	0.152	0.191	0.540	
SBP (mmHg)	M±SD	130.300 ± 4.332	140.70 ± 4.878	145.00 ± 6.581	150.566 ± 4.074	0.001
	SE	0.790	0.890	1.201	0.743	
DBP (mmHg)	M±SD	81.033 ± 4.230	84.333 ± 4.887	88.100 ± 4.171	91.233 ± 3.530	0.001
	SE	0.772	0.892	0.761	0.644	

Table (3): Clinical characteristic of Kidney functions, about investigation parameters in all studied groups, were shown as follows:

Clinical Variable		Group I (n=30) Non diabetics (Control)	Diabetics (N=90)			P-value*
			Group II (n=30) (Normoalbuminuria)	Group III (n=30) (Microalbuminuria)	Group IV (n=30) (Macroalbuminuria)	
HbA1c%	M±SD	5.366 ± 0.332	6.896 ± 0.547	8.143 ± 0.636	9.846 ± 1.362	0.001
	SE	0.060	0.099	0.116	0.248	
S. Cre. (mg/dl)	M±SD	0.761 ± 0.061	0.800 ± 0.082	0.870 ± 0.081	1.257 ± 0.160	0.001
	SE	0.011	0.015	0.014	0.029	
S. Urea (mg/dl)	M±SD	33.633 ± 3.547	35.166 ± 3.733	38.166 ± 2.320	47.633 ± 6.950	0.001
	SE	0.647	0.681	0.423	1.268	
ACR (mg/g)	M±SD	16.893 ± 2.670	18.206 ± 3.299	123.406±23.19	339.016±19.773	0.001
	SE	0.487	0.602	4.234	3.610	
eGFRcr (ml/min)	M±SD	99.966 ± 6.954	96.813 ± 4.707	86.440 ± 5.050	56.776 ± 5.971	0.001
	SE	1.269	0.859	0.922	1.090	
eGFR BTP (ml/min)	M±SD	8102.7 ± 727.56	7447.4±459.19	6666.3±345.72	5753.9±360.19	0.001
	SE	132.835	83.836	63.120	65.761	
eGFR Cys.C (ml/min)	M±SD	258.30 ± 15.236	250.56 ± 14.98	217.46 ± 9.543	177.93 ± 11.93	0.001
	SE	2.781	2.735	1.742	2.178	
S. Chol. (mg/dl)	M±SD	184.300±10.181	189.933±7.995	192.70±10.389	196.166 ± 9.577	0.001
	SE	1.858	1.459	1.896	1.748	
S. Tg. (mg/dl)	M±SD	92.866 ± 4.826	152.500±5.940	182.333±6.864	206.866 ± 8.528	0.001
	SE	0.881	1.084	1.253	1.557	
HDL (mg/dl)	M±SD	61.533 ± 4.621	57.100 ± 4.513	55.400 ± 4.047	52.633 ± 4.278	0.001
	SE	0.843	0.823	0.739	0.781	
BTP (pg/ml)	M±SD	617.066±68.182	692.56±33.713	797.63±44.446	991.866±82.985	0.001
	SE	12.448	6.155	8.114	15.151	
Cys. C (ng/ml)	M±SD	133.068±19.146	142.84±20.608	180.35±17.198	272.065±40.510	0.001
	SE	3.495	3.762	3.140	7.396	

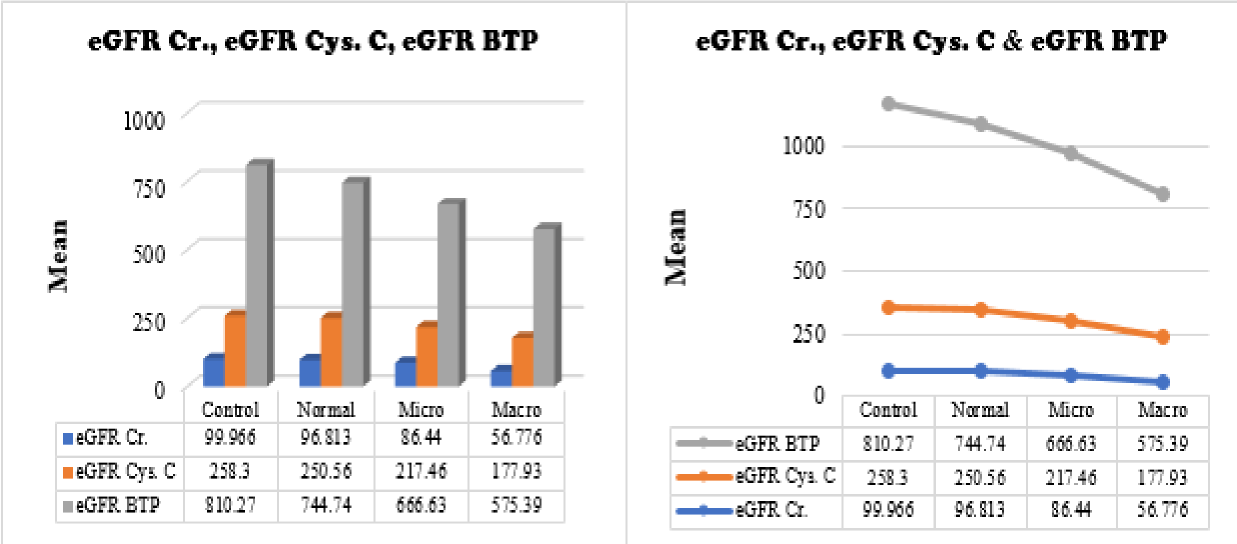

Figure (1): The mean of eGFR Cr. , eGFR Cys. C and eGFR BTP between the groups (GFR $_{BTP}$ multiplied by 0.1).

The correlation between S. BTP, S. Cys C, eGFR Cr., eGFR Cys. C and eGFR BTP in the four groupes was assessed using Pearson correlation coefficient. There is statistically significant correlation between the markers in healthy control, normoalbuminuria, microalbuminuria and macroalbuminuria groups. Regarding healthy control group, S. BTP had a statistically significant positive moderate correlation with eGFR BTP (r - 0.810, p <0.001) and S. Cystatin C with eGFR Cys. C (r - 0.752, p <0.001). eGFR Cr. had a statistically significant positive moderate correlation with eGFR Cys. C and eGFR BTP respectively (r 0.478, p <0.008), (r 0.482, p <0.007). as presented in table (4). Regarding normoalbuminuria group, S. BTP had a statistically significant positive moderate correlation with eGFR BTP (r - 0.630, p <0.001) and S. Cystatin C with eGFR Cys. C and eGFR BTP respectively (r - 0.658, p <0.001), (r - 0.613, p <0.001). eGFR Cr. had a statistically significant positive moderate correlation with eGFR Cys. C (r 0.472, p <0.008). as presented in table (5). Regarding microalbuminuria group, S. BTP had a statistically significant positive moderate correlation with eGFR BTP (r - 0.503, p <0.005) and S. Cystatin C with eGFR Cys. C (r - 0.709, p <0.001). as presented in table (6). Regarding macroalbuminuria group, S. BTP had a statistically significant positive moderate correlation with eGFR BTP (r - 0.613, p <0.001) and S. Cystatin C with eGFR Cys. C (r - 0.824, p <0.001). eGFR Cr. had a statistically significant positive moderate correlation with eGFR BTP (r 0.437, p <0.016). as presented in table (7).

Table (4): The correlation between Serum Beta Trace Protein, Serum Cystatin C, eGFR Cr., eGFR Cys. C and eGFR BTP in the healthy control.

Correlations							
Group	**Variable**	**r / Pvalue**	**BTP**	**Cys. C**	**eGFR Cr.**	**eGFR Cys. C**	**eGFR BTP**
Healthy Control	**BTP pg/ml**	r	1	0.126	-0.070	-0.072	-0.810**
		Pvalue		0.507	0.714	0.706	0.001
	Cys. C ng/ml	r	0.126	1	0.131	-0.752**	0.233
		Pvalue	0.507		0.489	0.001	0.216
	eGFR Cr.	r	-0.070	0.131	1	0.478**	0.482**
		Pvalue	0.714	0.489		0.008	0.007
	eGFR Cys. C	r	-0.072	-0.752**	0.478**	1	0.071
		Pvalue	0.706	0.001	0.008		0.708
	eGFR BTP	r	-0.810**	0.233	0.482**	0.071	1
		Pvalue	0.001	0.216	0.007	0.708	
** Correlation is significant at the 0.01 level (2-tailed).							

Table (5): The correlation between Serum Beta Trace Protein, Serum Cystatin C, eGFR Cr., eGFR Cys. C and eGFR BTP in the normoalbuminuria.

Correlations							
Group	**Variable**	**r / Pvalue**	**BTP**	**Cys. C**	**eGFR Cr.**	**eGFR Cys. C**	**eGFR BTP**
Normoalbuminuria	BTP pg/ml	r	1	-0.193	-0.066	-0.286	-0.630**
		Pvalue		0.308	0.730	0.126	0.001
	Cys. C ng/ml	r	-0.193	1	-0.259	-0.658**	0.613**
		Pvalue	0.308		0.168	0.001	0.001
	eGFR Cr.	r	-0.066	-0.259	1	0.472**	0.256
		Pvalue	0.730	0.168		0.008	0.171
	eGFR Cys. C	r	-0.286	-0.658**	0.472**	1	0.035
		Pvalue	0.126	0.001	0.008		0.854
	eGFR BTP	r	-0.630**	0.613**	0.256	0.035	1
		Pvalue	0.001	0.001	0.171	0.854	
** Correlation is significant at the 0.01 level (2-tailed).							

Table (6): The correlation between Serum Beta Trace Protein, Serum Cystatin C, eGFR Cr., eGFR Cys. C and eGFR BTP in the microalbuminuria.

Correlations							
Group	**Variable**	**r / Pvalue**	**BTP**	**Cys. C**	**eGFR Cr.**	**eGFR Cys. C**	**eGFR BTP**
Microalbuminuria	BTP pg/ml	r	1	0.322	0.167	-0.235	-0.503**
		Pvalue		0.082	0.378	0.210	0.005
	Cys. C ng/ml	r	0.322	1	-0.032	-0.709**	0.119
		Pvalue	0.082		0.868	0.001	0.531
	eGFR Cr.	r	0.167	-0.032	1	0.202	0.342
		Pvalue	0.378	0.868		0.285	0.064
	eGFR Cys. C	r	-0.235	-0.709**	0.202	1	0.325
		Pvalue	0.210	0.001	0.285		0.079
	eGFR BTP	r	-0.503**	0.119	0.342	0.325	1
		Pvalue	0.005	0.531	0.064	0.079	
** Correlation is significant at the 0.01 level (2-tailed).							

Table (7): The correlation between Serum Beta Trace Protein, Serum Cystatin C, eGFR Cr., eGFR Cys. C and eGFR BTP in the macroalbuminuria.

Correlations							
Group	**Variable**	**r / Pvalue**	**BTP**	**Cys. C**	**eGFR Cr.**	**eGFR Cys. C**	**eGFR BTP**
Macroalbuminuria	BTP pg/ml	r	1	0.095	-0.315	0.085	-0.613**
		Pvalue		0.616	0.090	0.656	0.001
	Cys. C ng/ml	r	0.095	1	-0.032	-0.824**	0.208
		Pvalue	0.616		0.866	0.001	0.270
	eGFR Cr.	r	-0.315	-0.032	1	0.128	0.437*
		Pvalue	0.090	0.866		0.501	0.016
	eGFR Cys. C	r	0.085	-0.824**	0.128	1	0.085
		Pvalue	0.656	0.001	0.501		0.654
	eGFR BTP	r	-0.613**	0.208	0.437*	0.085	1
		Pvalue	0.001	0.270	0.016	0.654	
** Correlation is significant at the 0.01 level (2-tailed).							

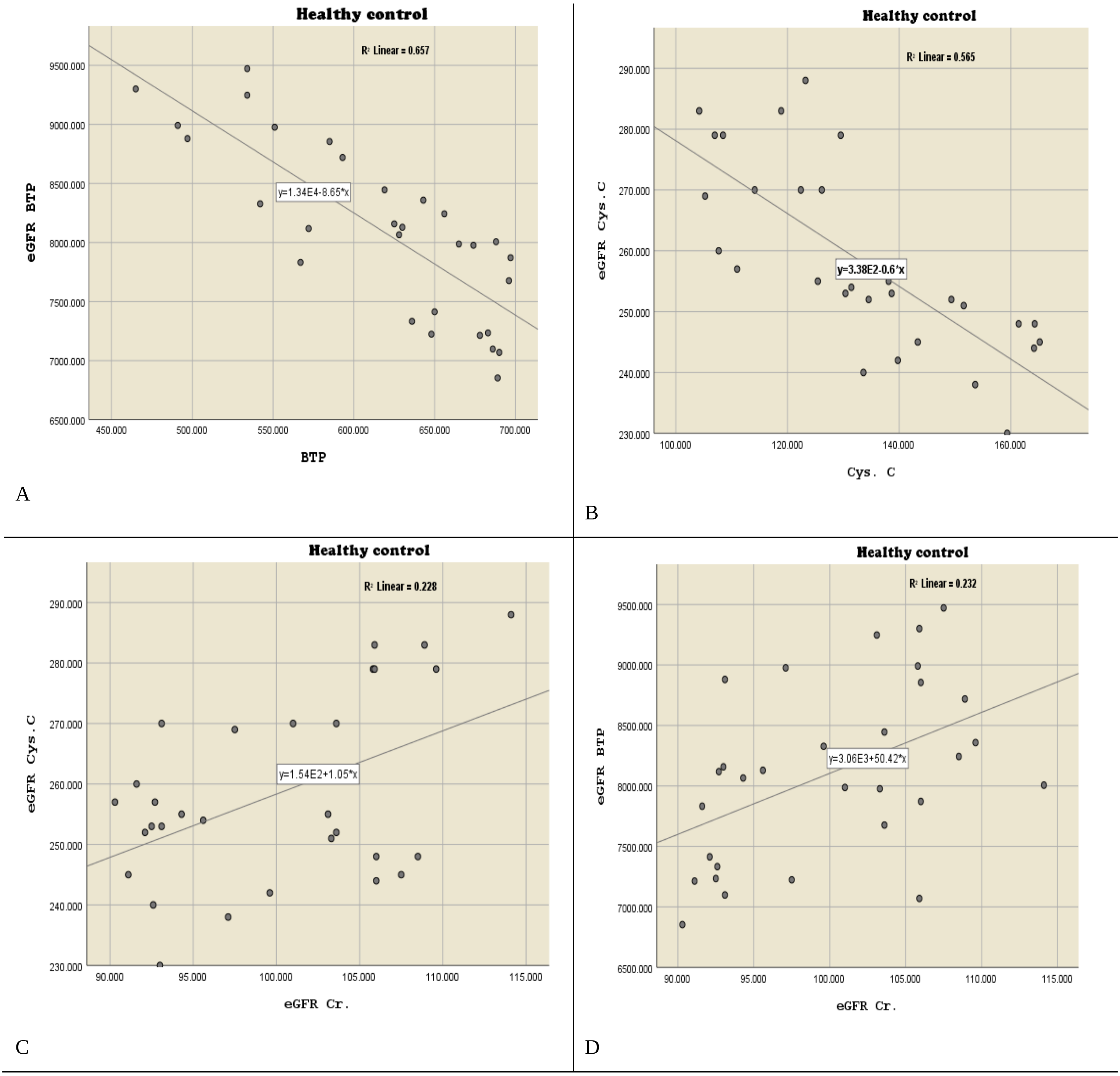

Figure (2): (A) Scattered dot diagram of correlation between Serum Beta Trace Protein with eGFR BTP, **(B)** Serum Cys. C with eGFR Cys. C , **(C)** eGFR Cr. with eGFR Cys. C, **(D)** eGFR Cr. with eGFR BTP in Healthy control group.

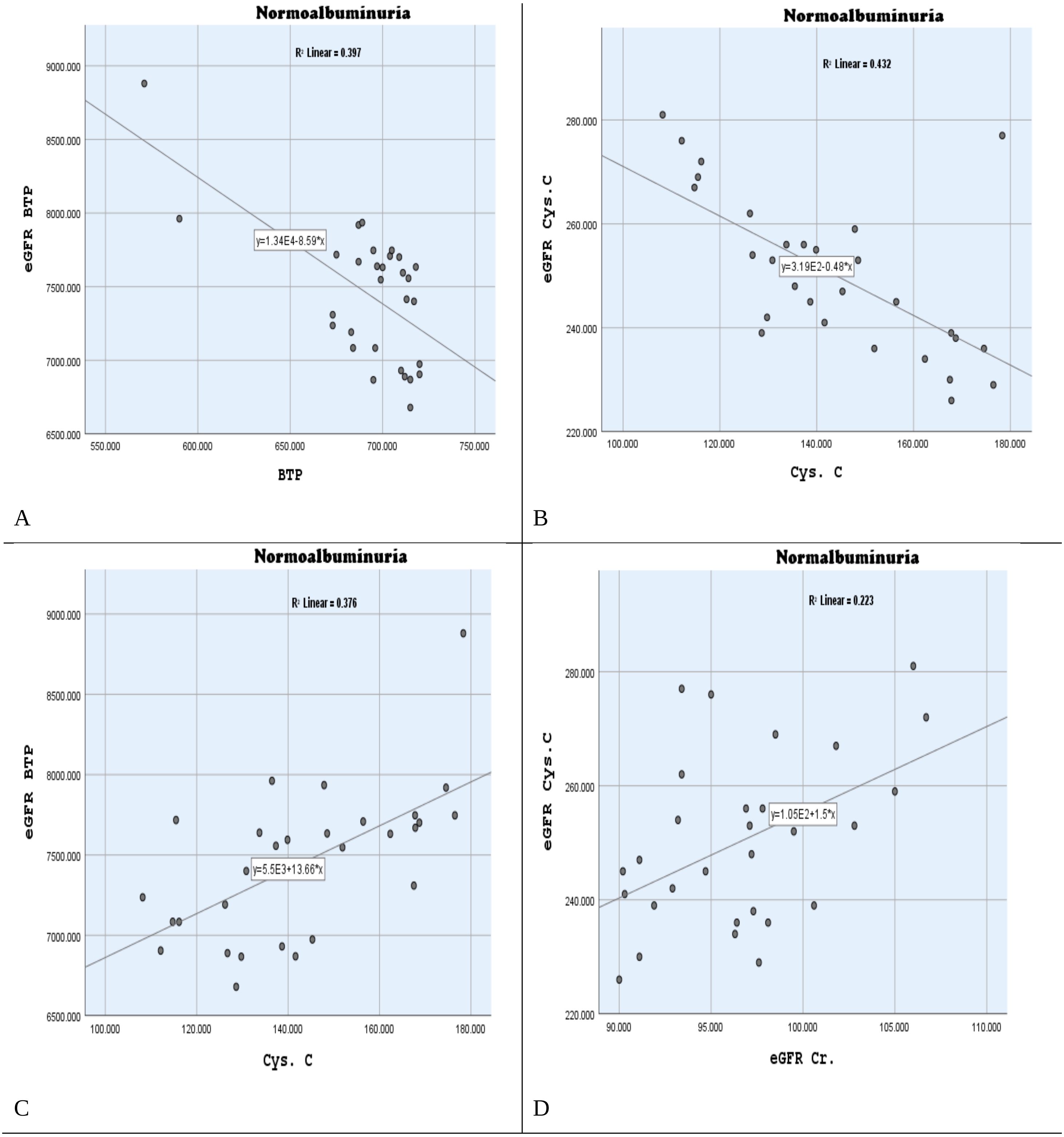

Figure (3): (A) Scattered dot diagram of correlation between Serum Beta Trace Protein with eGFR BTP, **(B)** Serum Cys. C with eGFR Cys. C, **(C)** Serum Cys.C with eGFR BTP, **(D)** eGFR Cr. with eGFR Cys. C in Normalbuminuria group.

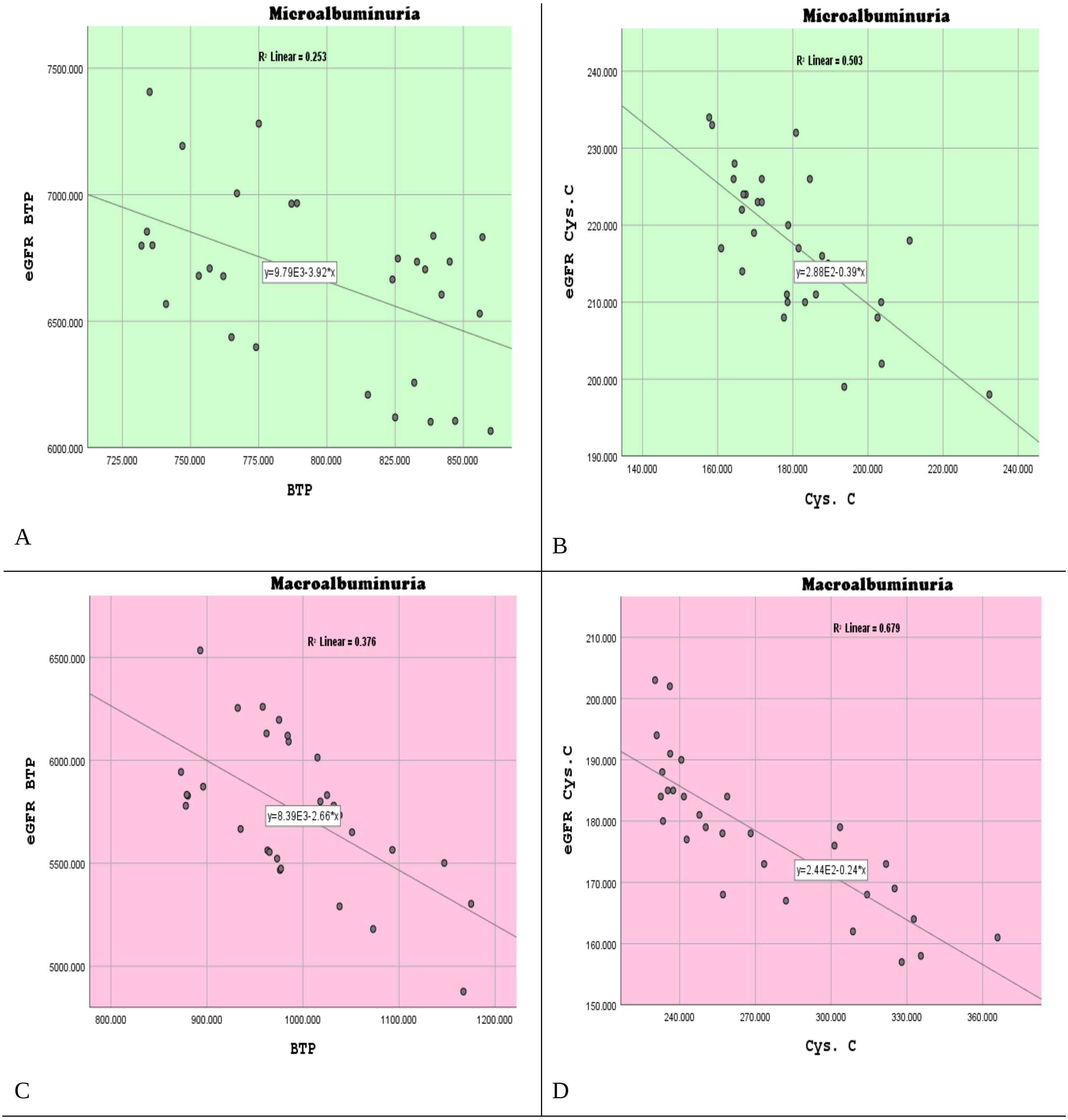

Figure (4): (A) Scattered dot diagram of correlation between Serum Beta Trace Protein with eGFR BTP, **(B)** Serum Cys. C with eGFR Cys. C in Microalbuminuria group, **(C)** Scattered dot diagram of correlation between Serum Beta Trace Protein with eGFR BTP, **(D)** Serum Cys. C with eGFR Cys. C in Macroalbuminuria group.

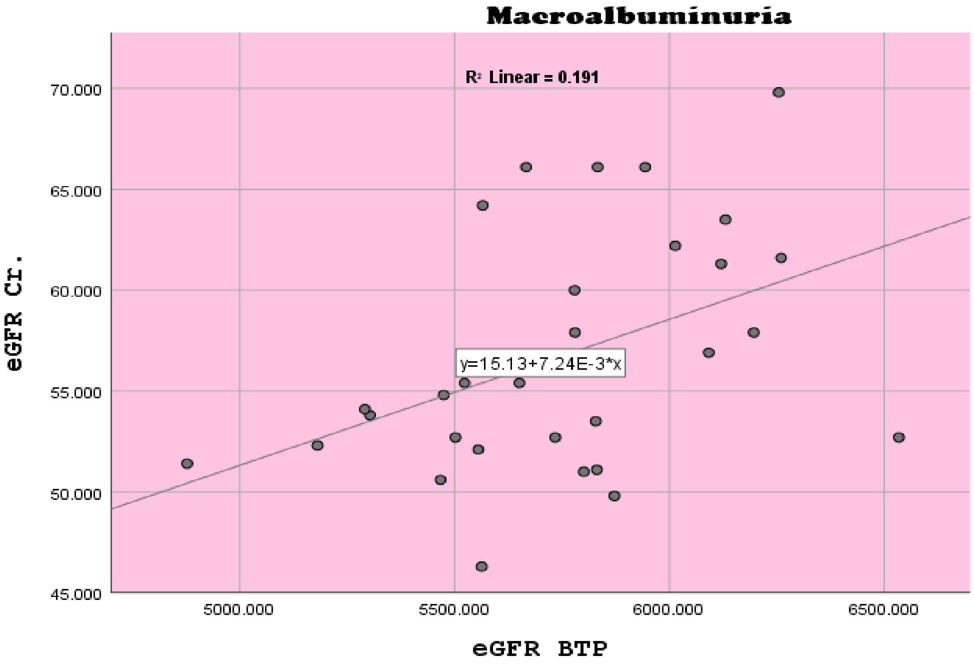

Figure (5): Scattered dot diagram of correlation between eGFR BTP with eGFR Cr. in Macroalbuminuria group .

Discussion

Diabetes can be linked to a variety of illnesses. If left untreated, it might eventually result in major health problems like heart disease, vascular disease, kidney disease, and even blindness **[10].** Researchers have concentrated their attention on early nephropathy diagnosis in type 2 diabetes since it requires a lot of time and resources, is expensive, and has a negative impact on a person's quality of life when chronic kidney disease develops. One of the primary causes of the last stage of renal failure, type 2 diabetes results in cirrhosis and the loss of nephron functioning **[11, 12].**

In the current study, as shown in the table (2), a P value for age (0.001) and the duration of diabetes for the groups (5-20 years) appears. As for sex, the percentage was male (54%) and the percentage for females (46%), and the P value for HbA1c was (0.001), and the P value of body mass index (0.001) , the P value of creatinine (0.001), and the P value of urea (0.001). through the table (3), that there are differences between the study groups P value (0.001) in the biomarker Serum Cystatin C, where macroalbumin levels were high (mean ± SD) (272.065 ± 40.510) compared to microalbumin group (180.358 ± 17.198), as well as levels of normalbumin group (142.849 ± 20.608) and the healthy control group (133.068 ± 19.146).

The study also showed that high levels of Cystatin C may be a sign of damage or early kidney failure among patients with type 2 diabetes **[13].** and it revealed that in the patient groups with macroalbuminuria, microalbuminuria, and normoalbuminuria, the amount of serum cystatin C was considerably greater than the normal level **[14].**

In line with previous research, individuals with T2DM had considerably increased serum cystatin C concentrations. Cystatin C concentration rises when nephropathy worsens in people with type 2 diabetes. Patients with macroalbuminuria exhibited significantly greater serum cystatin C levels compared to those with microalbuminuria and normoalbuminuria **[15].**

The results of Serum Beta Trace Protein were as shown in the table (3), where the significant difference was clear and large between the study groups P value (0.001), the macroalbumin group (mean ± SD) (991.866 ± 82.985), compared with the other groups, microalbumin (797.633 ± 44.446), normalbumin (692.566 ± 33.713) and healthy control (617.066 ± 68.182).

The studies, consistent with **[16, 17].** that found higher S.βTP levels in diabetic than control groups related to renal dysfunction in a T2DM patient in which S.βTP clearance is restricted by the kidneys. An considerable rise is noticed in the early stages of the illness because the elevated levels of S.βTP in the blood and urine correspond closely with the decline in glomerular filtration in individuals with CKD.

As it is clear from the results of eGFRcr, there is a difference in the results between the groups studied, as shown in the table (3) above, healthy control (mean ± SD) (99.966 ± 6.954), normabumin (96.813 ± 4.707), microalbumin (86.440 ± 5.050) and macroalbumin (56.776 ± 5.971). Low GFR is linked to a higher risk of renal failure, making it one of the greatest predictors of kidney function **[18].** There is a similar recent study showed a significant difference in the glomerular filtration rate (eGFR EPI) between the groups **[15].**

The results for eGFRcys.c show that there are differences between the results of the study groups as shown in the table (3) above, and this is explained by the fact that the estimate of eGFRcys.c depends on the level of cystatin in each group, healthy control (mean ± SD) (258.30 ± 15.236), normabumin (250.56 ± 14.982), microalbumin (217.46 ± 9.543) and macroalbumin (177.93 ± 11.933). meaning that the higher the cystatin, the higher the eGFRcys.c, in addition to that it depends on age and gender. consistent with previous studies **[19, 20].** As it is clear from the table (3) above for the results of eGFR BTP, there is a high difference between the studied groups, as shown in the figure above. was the average of the groups healthy control (mean ± SD) (8102.7 ± 727.56), normalbumin (7447.4 ± 459.19), microalbumin (6666.3 ± 345.72) and macroalbumin (5753.9 ± 360.19). To explain this, the estimate of eGFR BTP depends on the level of beta in each group, meaning that the higher the beta level, the higher the eGFR BTP. There are studies consistent with the findings from the aforementioned in diabetic nephropathy patients **[20, 21].**

As it is clear from the table (3) above, that GFR BTP is better than GFR Cr. And GFR Cys. in comparison between the studied groups, as it was noted in GFR BTP that there is a greater difference between the groups, what distinguishes GFR BTP and puts it better is that the clear differences between the totals, and also that it does not depend on the body mass of muscles, that is, there is no effect on the estimate glomerular filtration rate Beta Trace Protein.

Regarding healthy control group, S. BTP had a statistically significant positive moderate correlation with eGFR BTP (r - 0.810, p <0.001) and S. Cystatin C with eGFR Cys. C (r - 0.752, p <0.001). eGFR Cr. had a statistically significant positive moderate correlation with eGFR Cys. C and eGFR BTP respectively (r 0.478, p <0.008), (r 0.482, p <0.007). as presented in table (4). Regarding normoalbuminuria group, S. BTP had a statistically significant positive moderate correlation with eGFR BTP (r - 0.630, p <0.001) and S. Cystatin C with eGFR Cys. C and eGFR BTP respectively (r - 0.658, p <0.001), (r - 0.613, p <0.001). eGFR Cr. had a statistically significant positive moderate correlation with eGFR Cys. C (r 0.472, p <0.008). as presented in table (5). Regarding microalbuminuria group, S. BTP had a statistically significant positive moderate correlation with eGFR BTP (r - 0.503, p <0.005) and S. Cystatin C with eGFR Cys. C (r - 0.709, p <0.001). as presented in table (6). Regarding macroalbuminuria group, S. BTP had a statistically significant positive moderate correlation with eGFR BTP (r - 0.613, p <0.001) and S. Cystatin C with eGFR Cys. C (r - 0.824, p <0.001). eGFR Cr. had a statistically significant positive moderate correlation with eGFR BTP (r 0.437, p <0.016). as presented in table (7).

As the results were shown above, there is a correlation, and this has been confirmed by previous studies **[9].** it was found that there is a high correlation between eGFR BTP and BTP this is consistent with **[20].** that the correlation of eGFR BTP is associated with BTP, because BTP has proven to be a good diagnostic marker **[21].**

Likewise for GFR Cys. C, as there are previous studies **[22].** that support what we have reached, as GFR Cys.C is associated with cystatin C and with other markers.

Conclusion

1. the level of GFR βTP is marked decrease than GFR Cystatin C and GFR Cr. in early stage microalbuminuria cumbered with normoalbuminuria group, the level of GFR βTP is better than

GFR Cystatin C and GFR Cr. which may be considered as a predictive marker for the estimation of eGFR in type 2 Diabetic Nephropathy.

2. The results of the current study showed an inverse correlation between BTP and GFR BTP in healthy control group, normalbumin group, microalbumin group and macroalbumin group and a positive correlation between Cystatein C and GFR BTP in normalbumin group.
3. The results of the current study showed an inverse correlation between Cystatein C and GFR Cys.c in healthy control group, normalbumin group, microalbumin group and macroalbumin group.
4. The results of the current study showed a positive correlation between GFR Cr and GFR Cys.c and GFR BTP in healthy control group, a positive correlation between GFR Cr and GFR Cys.c in normalbumin group and a positive correlation between GFR Cr and GFR BTP in macroalbumin group.

Acknowledgments:

The authors would like to acknowledge the support of Al-Ameen University, Baghdad, Iraq for their valuable support.

References

1. Bansal, L. and A. Dhiman, *A Rationalized Overview of Diabetic Nephropathy.* 2022.
2. Chakraborty, D., et al., *Serum BTP concentrations are not affected by hepatic dysfunction.* BMC nephrology, 2018. 19: p. 1-6.
3. Handayani, R., et al., *Serum Beta-Trace Protein versus Glomerulus Filtration Rate as a Predictor for Kidney Function among Hypertensive Patients.* Indonesian Journal Of Clinical Pathology And Medical Laboratory, 2021. 27(2): p. 127-131.
4. Ebert, N. and M.G. Shlipak, *Cystatin C is ready for clinical use.* Current Opinion in Nephrology and Hypertension, 2020. 29(6): p. 591-598.
5. Leyssens, K., et al., *Beta-trace protein as a potential marker of acute kidney injury: a pilot study.* Kidney and Blood Pressure Research, 2021. 46(2): p. 185-195.
6. Kaufman, D., H. Basit, and S. Knohl, *Physiology, glomerular filtration rate (GFR).* SourceStatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, 2020.
7. Daniele, C., et al., *Transcutaneous measurement of glomerular filtration rate in rodents.* Diabetic Nephropathy: Methods and Protocols, 2020: p. 129-137.
8. Inker, L.A., et al., *New creatinine-and cystatin C–based equations to estimate GFR without race.* New England Journal of Medicine, 2021. 385(19): p. 1737-1749.
9. Inker, L.A., et al., *GFR estimation using β-trace protein and β2-microglobulin in CKD.* American journal of kidney diseases, 2016. 67(1): p. 40-48.
10. Singh, A.-K., et al., *Dipeptidyl Peptidase (DPP)-IV inhibitors with antioxidant potential isolated from natural sources: A novel approach for the management of diabetes.* Pharmaceuticals, 2021. 14(6): p. 586.
11. Control, C.f.D. and Prevention, *Chronic kidney disease in the United States, 2019.* Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, 2019. 3.
12. Lousa, I., et al., *New potential biomarkers for chronic kidney disease management—a review of the literature.* International Journal of Molecular Sciences, 2020. 22(1): p. 43.
13. Rao, X., et al., *Role of cystatin C in renal damage and the optimum cut-off point of renal damage among patients with type 2 diabetes mellitus.* Experimental and therapeutic medicine, 2014. 8(3): p. 887-892.

14. Elsayed, M.S., et al., *Serum cystatin C as an indicator for early detection of diabetic nephropathy in type 2 diabetes mellitus.* Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 2019. 13(1): p. 374-381.

15. Sapkota, S., et al., *Diagnostic accuracy of serum cystatin C for early recognition of nephropathy in type 2 diabetes mellitus.* International Journal of Nephrology, 2021. 2021.

16. Hebah, H.A., et al., *Beta-trace protein as an early predictor of diabetic nephropathy in type II diabetes.* Journal of The Egyptian Society of Nephrology and Transplantation, 2018. 18(3): p. 96.

17. Wajda, J., et al., *Does Beta-Trace Protein (BTP) outperform cystatin C as a diagnostic marker of acute kidney injury complicating the early phase of acute pancreatitis?* Journal of Clinical Medicine, 2020. 9(1): p. 205.

18. Sagoo, M.K. and L. Gnudi, *Diabetic nephropathy: an overview.* Diabetic Nephropathy: Methods and Protocols, 2020: p. 3-7.

19. Poge, U., et al., *β-trace protein is an alternative marker for glomerular filtration rate in renal transplantation patients.* Clinical chemistry, 2005. 51(8): p. 1531-1533.

20. El-Aarag, B., et al., *El T. Serum Beta-Trace Protein and Cystatin C as Biomarkers for Renal Dysfunction in Patients with Chronic Kidney Disease.* J Mol Biomark Diagn, 2018. 9(4): p. 9-12.

21. Dajak, M., et al., *Beta-trace protein as a marker of renal dysfunction in patients with chronic kidney disease: comparison with other renal markers.* Journal of Medical Biochemistry, 2010. 29(2): p. 66-72.

22. Hoek, F.J., F.A. Kemperman, and R.T. Krediet, *A comparison between cystatin C, plasma creatinine and the Cockcroft and Gault formula for the estimation of glomerular filtration rate.* Nephrology Dialysis Transplantation, 2003. 18(10): p. 2024-2031.