ORIGINAL ARTICLE

BETA TRACE PROTEIN AS A PREDICTIVE BIOMARKER OF CHRONIC KIDNEY DISEASE

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ABSTRACT

Keywords: Chronic kidney disease, beta-trace protein.

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Background: Chronic kidney disease (CKD) is a rapidly increasing world-wide public health problem. **Objective:** To estimate the level of Serum Beta-Trace Protein in patients with CKD and compare with normal subjects. **Patients and methods:** we include 90 subjects of them 70 patients suffering from CKD more than two years and 20 controls who admitted the department. **Results:** Age median of the patients was 30-53 years and 50 % of them were males. Patients with diabetes mellitus and hypertension were presented in 29 (41.4%) and 46 (65.7%) patients, respectively. Patients group had significantly higher creatinine (7.93 ± 2.67 vs. 1.11 ± 0.15 mg/dl; P< 0.001) and urea (113.87 ± 42.50 vs. 11.55 ± 2.34 mg/dl; P< 0.001), also, patients' group had significantly higher Beta trace proteins (69.18 ± 38.07 vs. 8.50 ± 4.80 mg/l; P< 0.001). Beta trace proteins was insignificantly lower among patients with DM comparison to those without DM. Also, patients with HTN had insignificantly lower Beta trace proteins in comparison those without HTN (71.63 ± 42.90 vs. 68.53 ± 35.55 mg/l; P= 0.67). Beta trace proteins had insignificant negative correlation with the age of patients (r= -0.19, P= 0.10), and positive correlation with urea (r= 0.11, P= 0.35) and creatinine (r= 0.20, P= 0.09). **Conclusion:** BTP might serve as an alternative endogenous marker for GFR, BTP may be a useful and reliable serum marker for identifying the magnitude of renal dysfunction in patients with CKD

INTRODUCTION

Chronic kidney disease (CKD) is a general term for heterogeneous disorders affecting the structure and function of the kidney (1). CKD results from many causes, including diabetes, glomerulonephritis, hypoxia, hypertension, infections, and polycystic kidney disease. CKD is associated with age-related renal function decline accelerated in hypertension, diabetes, obesity, and primary renal disorders (2) there are many predictive biomarkers can be used for chronic kidney disease. β-trace protein (BTP), which is known as lipocalin-type prostaglandin D synthase, it is a small protein. Like other low molecular weight proteins, (3) It is freely filtered by the glomerulus without secretion or reabsorption in renal tubules and it is almost completely excreted via the kidneys. Increased concentrations of BTP in serum reflect reduced clearance of the protein, assay of serum BTP is utilized to detect renal disease. β-Trace protein is a novel endogenous filtration marker of kidney function that is not removed during haemodialysis and may serve as a marker for residual kidney function. (4) This suggests the feasibility of LMWPs and namely BTP as a marker to screen for patients with GFR impairment.

We aimed in this study to estimate the level of Serum Beta-Trace Protein in patients with CKD and compare with normal subjects

PATIENTS AND METHODS

The present study is a case control study, carried out on 90 subjects, 70 patients (35Males, & 35 females) and 20 controls (11 males & 9 females) median age was (30-53years). Our inclusion criteria were 70 patients suffering from CKD more than two years including patients who are diabetic and hypertensive after taking history and carefully clinical examination by nephrologist with age median (30-53years), and exclusion criteria were subjects with pregnancy, chronic liver disease, autoimmune disease, infection and smoking.

Method:

Four ml of venous blood samples was withdrawn. Serum was collected by serum separator tube, where the samples were allowed to clot for 2 h at room temperature or overnight at 4°C before centrifugation for 15 min at 1000*g*. The serum was removed and aliquoted and stored at −20°C. Serum BTP was measured by ELISA kit based on double-antibody sandwich enzyme-linked immunosorbent assay technology

Ethical consideration

Informed consent was taken from every participant in this study and approval of the Medical ethical committee of Aswan University was taken.

Statistical analysis.

Data was collected and analyzed using SPSS 25. Continuous data was expressed in form of mean ± SD or median (range) while nominal data was expressed in form of frequency (percentage). Chi^2-test was used to compare the nominal data of different groups in the study while student t-test was used to compare mean of different two groups. Pearson correlation was used to determine the correlation between Beta trace protein with age, creatinine, and urea. ROC curve was used to determine accuracy of Beta trace protein in diagnosis of chronic kidney disease. Level of confidence was kept at 95% and hence, *P* value was significant if < 0.05.

RESULTS

We included 90 patients of them 70 patients had CKD (35Males, & 35 females) with mean age 40.91 ± 6.12 years with range between 30 and 53 years and fifty percent of them were males and 20 controls (11 males & 9 females) with mean age 39.58 ± 7.77 years with range between 20 and 55 years and majority (55%) of them was males. Patients and control groups had insignificant difference as regarding age (P= 0.33) and sex (P= 0.09). Table-1

Table-2 show that diabetes mellitus and hypertension were presented in 29 (41.4%) and 46 (65.7%) patients, respectively.

Table-3 show kidney function and Beta trace proteins among studied groups. It was noticed that patient's group had significantly higher urea (7.93 ± 2.67 vs. 1.11 ± 0.15 mg/dl; P< 0.001) and creatinine (113.87 ± 42.50 vs. 11.55 ± 2.34 mg/dl; P< 0.001) in comparison to the control group. Also, patients' group had significantly higher Beta trace proteins in comparison to control group (69.18 ± 38.07 vs. 8.50 ± 4.80 mg/l; P< 0.001).

Table -4 reveal that level of Beta trace proteins was significantly higher among males' patients in comparison to females' patients (88.27 ± 26.90 vs. 34.50 ± 19.25 mg/l; P= 0.02).

Table 5 reveal that level of Beta trace proteins was insignificantly lower among patients with DM comparison to those without DM (66.60 ± 37.22 vs. 71.76 ± 38.68 mg/l; P= 0.93). Also, patients with HTN had insignificantly lower Beta trace proteins in comparison those without HTN (71.63 ± 42.90 vs. 68.53 ± 35.55 mg/l; P= 0.67).

Table -6 shows that Beta trace proteins had insignificant negative correlation with the age of patients (r= -0.19, P= 0.10), and positive correlation with urea (r= 0.11, P= 0.35) and creatinine (r= 0.20, P= 0.09).

DISCUSSION

The identification of chronic kidney disease (CKD) patients at early stages of impairment of renal function may slow the progression of CKD and possibly reduce the number of incident patients who need the replacement of renal function. Beta-trace protein (BTP), also known as lipocalin prostaglandin D2 synthase, is a novel low-molecular-weight glycoprotein (5) that is being investigated for its use as a marker of GFR. It exhibits similar advantages to cystatin Cover serum creatinine, being independent of height, sex, age, and muscle mass, and showing increased sensitivity, particularly in the creatinine blind range (6).

In our study , we have used samples of Human serum `as Mudher et al and Ebert et al (7) who used serum samples to detect renal biomarkers as B –trace proteins whereas Piñero et al who obtained their samples from rat`s cerebro-spinal fluid. We have performed our research on subjects of average age 40.91 ± 6.12 for cases and 39.58 ± 7.77 for the controls in comparison to the average mean of 49 years in Donadio`s study of B trace protein in CKD patients and that of the subjects in the research of Hebah et al which was more than 18 years old (8).

Our study showed level of Beta trace proteins was insignificantly lower among patients with DM comparison to those without DM (P= 0.93) opposite to significant statistical difference between both diabetic patients and controls for BTP (P value < 0.005) in the study of Hebah et al and Mudher et al who revealed in their own research a significant correlation(6,8) (P< 0.05).

Our study revealed that level of Beta trace proteins was significantly higher among males' patients in comparison to females' patients (P= 0.02) in comparison with Filler et al who did not find an association between BTP and age in a cohort of pediatric patients with various renal diseases, although there was no correction for GFR and all participants were children(10).

In our study Patients and control groups had insignificant difference as regarding age (P= 0.33) and sex (P= 0.09). Whereas some studies describe higher βTP concentrations in adult men compared with women (11), most studies have shown no sex differences in children (12). BTP has not been shown to differ by sex in youth (13), whereas others report no sex differences (13).

Also in our study patients group had significantly higher urea (7.93 ± 2.67 vs. 1.11 ± 0.15 mg/dl; P< 0.001) and creatinine (113.87 ± 42.50 vs. 11.55 ± 2.34 mg/dl; P< 0.001) .Also Hebah et al (9) found that serum BTP was positively significant correlated with blood urea (P=0.043).According to Mudher et al `s study (7) ,The mean ± SD of BTP serum concentration in all cases had shown significant higher level than from its serum concentration in control group as what we revealed in our study .

CONCLUSION

BTP is a promising marker to assess glomerular and tubular function in adults. Increased concentrations of BTP in serum reflect reduced clearance of the protein. Beta trace proteins was significantly higher among males' patients in comparison to females' patients and insignificant negative correlation with the age of patients and positive correlation with urea and creatinine. Future studies are necessary to elucidate a potential clinical role for BTP.

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Table 1 Age and sex distribution among studied groups

	Patients group (n= 70)	Control group (n= 20)	*P* value
Age (years)	40.91 ± 6.12	39.58 ± 7.77	0.3
Range	30-53	20-55	3
Sex			0.0
Male	35 (50%)	11 (55%)	9
Female	35 (50%)	9 (45%)	

Data expressed as mean (SD), range and frequency (percentage). P value was significant if < 0.05

Table 2 Frequency of diabetes mellitus and hypertension among patients' group

	N= 70
Diabetes mellitus	29 (41.4%)
Hypertension	46 (65.7%)

Data expressed as frequency (percentage)

Table 3 Kidney function and Beta trace protein among studied groups

	Patients group (n= 70)	Control group (n= 20)	*P* value
Creatinine (mg/dl)	7.93 ± 2.67	1.11 ± 0.15	< 0.001
Urea (mg/dl)	113.87 ± 42.50	11.55 ± 2.34	< 0.001
Beta trace proteins (mg/l)	69.18 ± 38.07	8.50 ± 4.80	< 0.001

Data expressed as mean (SD). P value was significant if < 0.05

Table 4 Level of Beta trace proteins based on sex of patients

Sex of the patients	Mean
Male	88.27 ± 26.90
Female	34.50 ± 19.25
***P* value**	0.02

Data expressed as mean (SD). P value was significant if < 0.05

Table 5 Levels of Beta trace proteins based on presence of DM and HTN

	DM	**HTN**
Yes	66.60 ± 37.22	68.53 ± 35.55
No	71.76 ± 38.68	71.63 ± 42.90
***P* value**	0.93	0.67

Data expressed as mean (SD). P value was significant if < 0.05. DM: diabetes mellitus; HTN: hypertension

Table 6 Correlation of Beta traces proteins with age, urea, and creatinine

Correlations of Beta trace proteins with	R	*P*
Age (years)	-0.19	0.10
Urea (mg/dl)	0.11	0.35
Creatinine (mg/dl)	0.20	0.09

Data was expressed as r (correlation coefficient), P (significance of correlation). P value was significant if < 0.05