



Original Research Article

Can proteinuria be used as a routine diagnostic aid for psychological stress?

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ABSTRACT

Introduction & Objectives : Diagnosis of stress often requires measurements of expensive, invasive and cumbersome stress markers. Previous studies have reported correlation of protein: creatinine ratio with anxiety and depression. The present research was designed to explore the performance of urinary protein and microalbumin or both as diagnostic aid for stress.

Materials and Methods: The present research was an OPD/IPD based case control research where 120 patients, without any other obvious illness, and 106 healthy controls, were assessed for stress (by PSLE) . Urinary protein and creatinine were estimated by Vitros 5.1 fusion analyzer. Statistical package for social sciences version 21.0 (SPSS v 21.0) was used for data analysis.

Results : A significant correlation was observed between PCR, ACR and PSLE ($p < 0.05$)

Interpretation & Conclusion: The study showed significant correlation between PSLE and urinary protein and microalbuminuria in comparison to controls.

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1. Introduction

Psychological stress is defined as homeostatic adjustment induced by psychological factors which may involve several social and emotional stressors.¹ Major life events can act as stressors and associated with stress related health outcomes.²

Stress should be diagnosed as early as possible. Serious health problems may be caused due to negligence of stress. It also has indications for kidney disease.³ Early recognition of stress is significant to prevent stress related alterations in kidney. Diagnosis of stress often requires measurements of expensive, invasive and cumbersome stress markers mostly in blood specimens. Till now there is no stress marker that can be used universally. This necessitates the need for simple, inexpensive and non-invasive universal stress

markers that can be done in any primary health care set up.

Proteinuria is defined as the existence of significantly increased amount of proteins in the urine. Normal adults excrete roughly less than 150 mg/dl of protein in the urine. It is conventional marker of renal disease and includes glomerular and other tubular proteins. It has been associated with different physiological and pathological conditions.⁴

However, less attention has so far been paid to the diagnostic role of urinary protein in psychological stress. There is paucity of data associating stress with urinary proteins.

Besides, it is not known whether stress induced due to major life events a person encounters in his life can result in an alteration in urinary protein excretion in otherwise healthy individuals. Previous studies have correlated protein creatinine ratio with anxiety and depression.⁵ Another study correlated albuminuria with anxiety and depression.⁶

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However it is unclear whether stress without significant anxiety and depression also leads to an increase in excretion of albumin or other proteins.

1.1. In consideration of the above, the present research was designed to explore

Whether stress generated due to major life events is associated with proteinuria, and 2) Whether proteinuria, microalbuminuria or both can be used as a diagnostic aid for stress.

2. Materials and Methods

The present research was a OPD /IPD based case control research, where we randomly examined patients belonging to 20-50 years age group, visiting the psychiatric OPD of Subharti Medical College and hospital. The presumptive stressful life events scale (PSLE) was used to assess the patients subjectively where 120 patients were assessed for stress without any other obvious illness and 106 other healthy age and sex matched controls that were without any significant stress.

Patient with an established diagnosis of nephropathy, neuropathy, retinopathy, hypertension, cardiovascular diseases, as well as smokers, alcoholics, were excluded. The institutional ethical committee and research council provided the ethical clearance. After obtaining written informed consent, the individuals were evaluated with detailed past history, clinical history and family history and subsequently assessed by psychiatric stressful life events (PSLE) scale.

Spot urine sample of patients were collected in sterile urine container, then centrifuged and stored at minus 20°C. For urinary creatinine analysis 1 volume of spot sample was mixed with 20 volumes of reagent grade water. Vitros 5.1 Fusion chemistry system which is from Orthoclinical diagnostics by Johnson and Johnson USA was used for estimation of urinary protein and creatinine of all the subjects. Statistical package for social sciences version 21.0 (SPSS v 21.0) was further used for data analysis. A p value < 0.05 was considered to be statistically significant.

3. Results

Of the 226 individuals assessed, 120(53.09 %) were cases and 106(46.91%) were controls. Further, among the cases 71(59.2%) were males and 49(40.8 %) were females and in controls 61(57.5 %) were male and 45(42.5 %) were females. The cases had significantly higher values of protein: creatinine ratio (PCR) as compared to controls (Table 1). On analysing the correlation of PCR with PSLE among the cases in our study group, it was found that there existed a significant correlation of PCR with PSLE ($p < 0.05$). PCR was strongly correlated with PSLE with a correlation coefficient of 0.768 [Figure 1]. On analysing

the correlation of ACR with PSLE, it was found that there existed a significant correlation of ACR with PSLE ($p < 0.05$). ACR is moderately correlated with PSLE with a correlation coefficient of 0.548 [Figure 2]

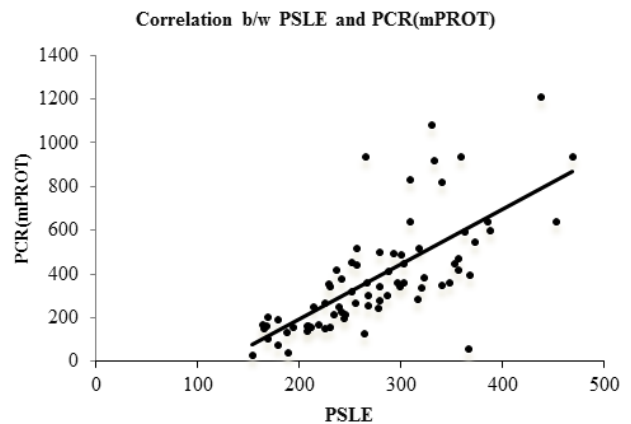


Fig. 1: Correlation between PSLE and ACR

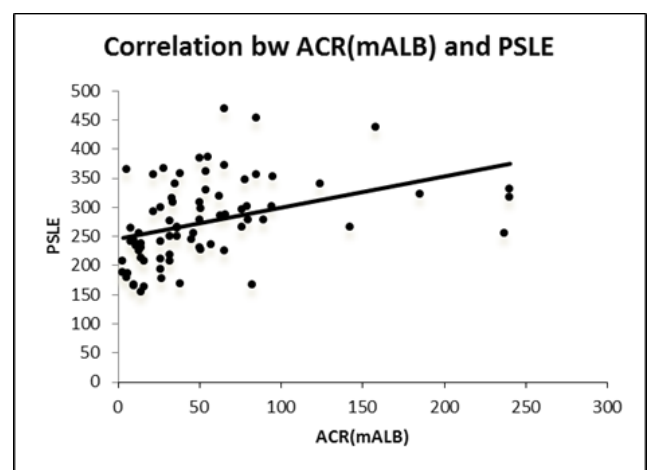


Fig. 2: Correlation between PSLE and ACR

4. Discussion

Present study was designed to explore if proteinuria can be used as a routine diagnostic aid for assessment of psychological stress.

This study showed that raised protein: creatinine and albumin:creatinine ratio were associated with significant life event stress scores in cases, in comparison to controls. Previous studies have also reported increased proteinuria in stressed individuals.⁵ No study till date however correlated protein: creatinine or albumin: creatinine ratio with PSLE. Ratnakar et al⁵ explained depression, anxiety and proteinuria in primary caregivers of patients having cancer. Dalui et al⁶ explained depression, anxiety and

Table 1: Values of PCR, ACR & PSLE in mean \pm SD among cases and controls

	Group		P value
	Cases	Controls	
PCR (in mg/g of creatinine)	382.96 \pm 252.92	91.77 \pm 45.22	< 0.0001
ACR(in mg/g of creatinine)	54.05 \pm 52.29	10.73 \pm 9.78	<0.0001
PSLE score	275.69 \pm 71.25	82.08 \pm 27.23	<0.0001

albuminuria in primary caregivers of patients having mental illness. Psychological stress thus can be associated with caregiving to mentally ill and cancer patients and can be one of the determinants of protein excretion rate in otherwise healthy subjects.

The urinary protein: creatinine (UPr:Cr) ratio, was significantly higher in the cases in comparison to controls as demonstrated in previous studies.^{5,6} Koner et al⁵ demonstrate that family caregivers of the advanced cancer patients undergo anxiety and depression associated with stress which might leads to increased oxidative stress and glomerular permeability to particular proteins which are otherwise not present in healthy individuals. There are few other reports which show that stress causes proteinuria.^{7,8} Spearman rank correlation coefficient in cases indicates a correlation between Upr:Cr, Ualb:cratio and PSLE scores. PSLE is more strongly correlated with PCR as compared to ACR. Hence, from the results, it was clear that an increment in the urinary protein: creatinine ratio is associated with an increment in the stress factors (assessed by PSLE). Psychological stress due to major life events probably affects the renal system at the level of tubules, as suggested by its effect primarily on proteinuria, as compared to albuminuria. This finding is supported by the fact that in case of glomerular proteinuria albumin is the predominant protein. Ratnakar et al⁵ have demonstrated that anxiety, depression is the cause of increased proteinuria. Glomerular alterations or defects result in albuminuria, so the mechanism of proteinuria must be different. The concept, that glomerular filtration is restricted because of the size and charge barrier of the glomerular basement membrane, is widely accepted.

We propose a hypothesis that psychological stress lead s to sympathetic activation, which in turn can lead to renal arterial/arteriolar vasoconstriction resulting in less blood flow to kidneys. Less blood flow means less ATP that in turn leads to alteration in charge distribution across the membrane Na-K-ATPase pump. This leads to influx of some other proteins which are normally not present in the urine. As cases as well as controls were extensively screened for other causes of proteinuria, this marked difference between the two could be due to stress induced by major life events.

During interview, none of the patients reported any significant anxiety or depression along with stress; hence the contribution of anxiety or depression appears to be less. The cases were apparently normal and they did not report any other obvious illness. The underlying mental stress because

of major life events may induce psychological stress where proteinuria could be one of the markers. Routine stress analysis is costly and requires trained staff and tedious standardization. Microalbumin estimation is costly, while micro protein estimation is cheap, and can be done by any technician even in a small primary care set up.

The major limitation of this study is that the estimated urinary total protein includes several proteins including albumin. This makes it impossible to identify the part of the kidney involved. Besides, without performing electrophoresis, or its subsequent processing, one cannot identify the type of proteins involved. Again , performing basic electrophoresis also involves concentrating the urine sample, process which is cumbersome for routine biochemistry lab. Further, identifying all the proteins may involve immunological tests and protein sequencing. Due to feasibility issues, it was not possible to collect the urine of subjects three times on different days. Hence, the physiological variation [high intra-individual CV (30-50%) and diurnal variation (50-100%)⁹ could affect the protein excreted in urine although we tried to compensate for variation by taking protein/creatinine ratio.

Microalbuminuria is often confused with proteinuria. It is important for consultants to be aware of the difference between proteinuria and microalbuminuria. Protein estimation also has the potential of being used as marker for stress in population studies. Further studies are required to explore the possibility of using proteinuria for exploring work related stress and may unfold categories of stress where proteinuria is associated with certain types of stress.

5. Conclusion

The study showed that there was significant correlation between PSLE and urinary protein and Microalbumin in comparison to controls. However, between Microalbumin and urinary total protein measurement, it is urinary protein that may provide superior diagnostic information. In order to fine tune our understanding of proteinuria in these cases including the likely mechanism involved, we propose the identification of the proteins excreted.

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8. Conflict of interest

None.

9. Ethical approval

The institutional ethics committee approved the research.

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