Clinical and Biochemical Correlation of Microalbuminuria in Rheumatoid Arthritis Patients

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Abstract

Objective: There are very few well-known studies regarding the significance of microalbuminuria in Rheumatoid arthritis patients and its clinical and biochemical correlations with disease activity. The present study is therefore aimed to determine the presence of microalbuminuria in Rheumatoid arthritis patients and to correlate with different parameters of disease activity.

Methods: This Cross-sectional observational study was conducted on purposively selected patients who attended Department of Medicine, Mymensingh Medical College Hospital, Mymensingh during the period from April, 2017 to March, 2018. 110 cases with Rheumatoid Arthritis (RA) meeting the exclusion and inclusion criteria were interviewed, examined and investigated to find out correlation of clinical and biochemical parameters of disease activity with presence of microalbuminuria in Rheumatoid arthritis patients.

Results: Out of 110 RA patients, 30 (27.3%) were male and 80 (72.7%) were female with a mean age of patients (42.94 ± 4.87) years in microalbuminuria positive group and (39.48 ± 6.19) years in microalbuminuria negative group. 33(30%) cases (25 female and 8 male) had microalbuminuria positive. Duration of morning stiffness was significantly longer in patients with microalbuminuria positive. Out of 33 patients positive for microalbuminuria, 27 patients had morning stiffness lasting more than 60 min. Mean number of joints involved was 18.12 ± 3.21 in microalbuminuria positive group (P<0.001). Mean ESR in microalbuminuria positive patients was 88.00 ± 23.14 mm in 1st hour (P<0.001). Mean CRP in microalbuminuria positive patients was 42.90 ± 12.01mg/l (P<0.001). Disease Activity Score (DAS) is higher in microalbuminuria positive patients (4.92±1.18) than negative patients (3.36±1.06) which is statistically significant (p<0.001).Among 33 microalbuminuria positive patients,18 patients had evidence of joint erosion on X ray(P<0.001).

Conclusion: RA patients having microalbuminuria were found significant clinical and biochemical correlation with severe disease activity. Microalbuminuria may be routinely measured in all Rheumatoid arthritis patients to detect renal involvement in an incipient stage to minimize disease morbidity.

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Keywords: C reactive protein (CRP); Erythrocyte sedimentation rate (ESR); Microalbuminuria; Rheumatoid arthritis, Disease activity score (DAS score).

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Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by joint swelling and tenderness as well as destruction of synovial joints, leading to severe disability and premature mortality.[1]Worldwide prevalence of RA is estimated to be between 0.3 to 1.5%. Various study in India suggests that, prevalence of RA is around 0.65-0.75%. The peak age of onset is around 50 years of age and is morecommon in female with female to male ratio is 3:1.[2]Microalbuminuria or dipstick negative albuminuria is conventionally defined as urinary albumin excretion between 30-300 mg/24 hours for timed 24 hours urine collections or between 20-200 mg/L for untimed random samples.[3] Microalbuminuria is a marker of widespread vascular damage. Various studies have shown that microalbuminuria is correlated with increased risk for renal and cardiovascular mortality and morbidity in diabetes mellitus, hypertension, acute myocardial infarction and some asymptomatic elderly patients.[4]But the significance of microalbuminuria in RA and its correlation with disease activity is not much studied. It is hypothesized that microalbuminuria and subclinical renal damage are frequent in RA patients particularly in those with severe and longstanding disease. Urinary albumin measured by immune turbimetric method may be a simple, noninvasive and sensitive test to detect early subclinical renal dysfunction. In patients with RA there is a high prevalence of renal impairment, with evidence of reduced glomerular filtration and tubular function. This has been considered due to direct effects of the disease on the kidneys, or the action of nephrotoxic drugs, or both.[5]Various morphological and histological findings in kidneys have been described and renal disease is presumed to be a frequent cause of death in RA.[6] Therefore, it would be useful to identify those at risk of developing clinical nephropathy at the earliest possible time. However, subclinical renal dysfunction is not uncommon in RA, and many of these patients with incipient nephropathy are not detected by routine laboratory tests including urinary total protein. The advent of assays sensitive and specific for urinary albumin has enabled the detection of glomerular abnormalities at an earlier stage in patients without clinical renal impairment.[7]Patients at risk of developing renal dysfunction might therefore be detected earlier by the presence of microalbuminuria. Furthermore, microalbuminuria may also indicate inflammatory state and disease activity of RA. If microalbuminuria is found to be associated with increased disease activity as well as early renal involvement, adequate measures may be taken promptly. This will improve total outcome of RA patients. As a result, the present study was designed to find out the correlation of microalbuminuria with RA through some common clinical and biochemical parameters.

Methods

Study design and settings

It was a cross-sectional observational study conducted at Department of Medicine, Mymensingh Medical College Hospital, Bangladesh. Total duration of study was one year (April 2018 to March 2019).

Study population

Patients aged >18 years who attended at Department of Medicine, Mymensingh Medical College Hospital with Rheumatoid Arthritis during the study period (Diagnosed by NEW 2010 ACR – EULAR Diagnostic criteria) were included in the study.[8] Purposive type of convenient sampling method was followed. Total 110 Rheumatoid Arthritis patients were enrolled in the study based on inclusion and exclusion criteria. Patients with hypertension, Diabetes Mellitus, Renal disease, pregnancy, prolonged fever due to any cause were excluded from study.

Laboratory methods

Random urine sample (5 ml) was collected from each patient usually 3-4 hours after last micturition and was sent to laboratory immediately. Quantitative measurement of urine albumin was done by immunoturbidimetric method using MALB Kidney Disease Assay Kit (Made in China) and Bioscience Chemical Analyzer (Made in Germany)[9]. Urinary albumin amount 20-200 mg/dl was defined as urinary microalbuminuria.

Data collection and analysis

Detailed history was taken from each patient including age, sex, resident, duration of morning stiffness, number of joints involvement includes swollen joints, H/O fever, weight loss, anorexia. Physical examinations included blood pressure measurement, number of tender joints, DAS-28 score (calculated using online calculator). Blood samples of all the patients were obtained for Erythrocytic Sedimentation Rate (ESR), C-Reactive protein (CRP). Relevant data from history, physical examination and investigations were recorded in predesigned questionnaire. After correcting or discarding all irrelevant and incorrect data, they were analyzed using SPSS version 25. Quantitative data were expressed as mean and standard deviation and comparison done by unpaired t test. Qualitative data were expressed as frequency and percentage and comparison carried by Chi-square test. A probability (p) value of <0.05 was considered statistically significant.

Ethical aspects

Informed written consent was obtained from all patients before enrollment in the study. Blood samples were collected through minimally invasive venipuncture procedure. The study was done with prior approval from "Institutional Review Board (IRB)" of Mymensingh Medical College Hospital. There was no conflict of interest.

Results

Table I illustrates that most of the patients had <15 joints involvement with mean number of joints involvement was 13.4±5.06. Out of 110 patients, 33 (8 male and 25 female) were found microalbuminuria.

Table I: Number of joints involved and presence of microalbuminuria in RA patients (n=110).

Number of patients	Number of joints involved	Percentage (%)	
40	<10	36.36	
35	11-15	31.82	
19	16-20	17.27	
16	>20	14.55	
Mean±SD	13.4±5.06		
	Present	Absent	
Microalbuminuria	33	77	
	Male: 8, Female: 25	Male: 22, Female: 55	
Morning stiffness	Number of patients	Microalbuminuria	
		Present	Absent
<30 minutes	12	3	9
31-60 minutes	18	3	15
>60 minutes	80	27	53

Table II reveals that mean CRP in microalbuminuria positive patients was 42.90 mg/L whereas in microalbuminuria negative patients was 21.75 mg/L. The difference was statistically significant (p<0.001).

Table II: Association of CRP levels (mg/L) with presence of microalbuminuria

CRP (mg/l)	Number of patients	Microalbuminuria (mg/dl)		P Value
		Present (%)	Absent (%)	
<10	45	0	45 (100)	
11-20	14	2 (14.3)	12 (85.7)	
21-40	20	11 (55.0)	9 (45.0)	<0.001
>41	31	20 (64.5)	11 (35.5)	
Mean CRP		42.90	21.75	

P value was calculated using unpaired t test.

Table III reveals association of Disease Activity Score (DAS) in RA patients with presence or absence of microalbuminuria. Here patients with microalbuminuria measured mean DAS 4.92 whereas patients without microalbuminuria had mean DAS 3.36. The difference was statistically significant (p<0.001)

Table III: Association of Disease Activity Score (DAS) with Microalbuminuria (n=110)

DAS(Score)	Number of patients	Microalbuminuria		P value
		Present (%)	Absent (%)	
<1.6	0	0	0	
<2.4	12	2(16.7)	10(83.3)	
2.4-3.7	49	3(6.1)	46(93.9)	<0.001
>3.7	49	28(57.1)	21(42.9)	
Mean DAS		4.92	3.36	

P value was calculated using unpaired t test.

Table IV illustrates association of various study parameters with microalbuminuria in rheumatoid arthritis patients. Statistically significant association was found regarding number of joint involvement (p<0.001), Mean ESR (<0.001), Mean CRP (<0.001), DAS score (<0.001), number of eroded joints (<0.001). No association was found in relation with age of the patients (p=0.094), sex (p=0.64) and morning stiffness (p=0.161).

Table IV: Different study parameters in relation to microalbuminuria

Study parameters	Microalbuminuria		P value
	Present	Absent	
Age in years (Mean±SD)	42.94±4.87	39.48±6.19	0.094*
Sex (Male:Female)	8:25	22:55	0.64*
Morning stiffness, n(%)	26 (23.64%)	54 (49.09%)	0.161*
No. of joints involved	18.12±3.21	11.38±4.30	<0.001†
Mean ESR ±SD (mm in 1st hour)	88.00±23.14	51.16±24.39	<0.001†
Mean CRP±SD (mg/l)	42.90±12.01	21.75±20.39	<0.001†
DAS Score	4.92 ± 1.18	3.36 ± 1.06	<0.001†
Joint Erosion (Number)	18	15	<0.001†

*p value was calculated using chi-square test. † p value was calculated using unpaired t test.

Discussion

The present study was undertaken to evaluate the association of microalbuminuria with rheumatoid arthritis and to determine the correlation of microalbuminuria with ESR, CRP, DAS score and number of joints involved. Our study revealed that the relative frequency of microalbuminuria in patients with Rheumatoid Arthritis was 33%, which was similar to other studies like Pederson LM et al. and Bhatt G et al.[10,11] The increased albumin excretion can be accounted for by either effect of systemic inflammatory rheumatoid disorders on vascular permeability or nephrotoxic side effects of treatment. Patients with RA are at risk of developing renal complications and proteinuria increases the mortality rate.[6] The present study supports the presence of pathological albuminuria in many RA patients without a history of renal dysfunction, hypertension, or diabetes mellitus. Our findings are consistent with earlier reports concerning subclinical renal dysfunction in RA.

From the present data, it implies that microalbuminuria may be a marker of severe disease activity. In this study the presence of microalbuminuria correlated significantly with ESR. But this does not correlate with findings by Pederson et al.[10] This is partially explained by the fact that some patients with normo-albuminuria had increased values of ESR for reasons other than RA. According to our study, mean CRP was (42.90 ± 12.01) mg/l in microalbuminuria positive patients as compared to (21.75 ± 20.39) mg/l in microalbuminuria negatives ($P<0.001$). Since both ESR and CRP are indicators of severity of the disease, presence of microalbuminuria may also indicate severe disease. Low grade inflammation as represented by CRP levels was significantly related to the presence of microalbuminuria.[12] Similar results were obtained by Pederson et al, who found that mean CRP was 112 (16-1615 nmol/l) and CRP was significantly correlated with urinary albumin:creatinine ratio (ACR). Bhatt et al. also found that microalbuminuria was associated with significantly higher CRP values. Microalbuminuria and subclinical renal damage are frequent in RA, particularly in those with severe disease. A subclinical renal involvement may not be revealed by routine laboratory tests such as serum creatinine.[11,13]

This study suggests that microalbuminuria may be a more sensitive and earlier predictor of disease severity in rheumatoid arthritis. It may serve as a useful tool for the diagnosis of renal involvement and severe RA without overt clinical nephropathy. However, the long-term renal prognosis in patients with microalbuminuria may require further larger longitudinal studies.

Conclusion

The study may suggest that presence of microalbuminuria indicates severe disease activity. Also, microalbuminuria is a sensitive indicator of increased renal vascular permeability in Rheumatoid Arthritis patients. So, immunological methods for detecting microalbuminuria should routinely be considered in all rheumatoid arthritis patients to detect renal involvement in its initial phase in order to devise the most appropriate treatment.

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