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RESEARCH LETTER

Oxidative stress in patients with rheumatoid arthritis: A cross-sectional study

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Rheumatoid arthritis (RA) is an autoimmune inflammatory disease which usually involves peripheral joints. There is a well-recognized connection between oxidative stress and inflammatory processes in RA. Oxidative stress is produced either by increased production of reactive oxygen species, decreased antioxidant defense, or a combination of both. There are inconsistent findings in the published literature regarding plasma malondialdehyde and superoxide dismutase levels in RA patients[1, 2]. This study aimed to compare the plasma malondialdehyde and superoxide dismutase levels between patients with or without RA.

This cross-sectional study was done in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University, Dhaka. Thirty patients with RA were enrolled in the rheumatology outpatients who had the confirmed diagnosis for at least one year. Thirty non-RA subjects were recruited purposively from the patients, relatives, or the hospital staff. Subjects with pregnancy and cardiovascular, cerebrovascular, respiratory, hepatic, renal, thyroid, irritable bowel syndrome, malignancy, and neuropsychiatric diseases were excluded. Other exclusions included acute or chronic inflammation, infection, recent major surgery, consumers of smoked or smokeless tobacco products, and those with antioxidant supplementations. Informed written consent was duly obtained from each subject prior to data collection.

Subjects were asked to be seated in a comfortable room and to take a 5-minute rest. Relevant history and physical examination findings were recorded in a questionnaire. Body mass index was calculated from the measured height and weight. Four mL of venous blood was collected in two vacuum tubes. One tube with 2 mL of blood was taken to the hematology department to estimate the complete blood count and erythrocyte sedimentation rate. Another tube with 2 mL of blood was brought to the Physiology Department and centrifuged at 3000 rpm for 15 minutes at 4° C, and plasma was collected in two tubes and labeled for identification. Then, all the samples were preserved at -20° C for the estimation of plasma malondialdehyde and superoxide dismutase levels using a malondialdehyde- ELISA kit and total superoxide dismutase assay kit (Elabscience Biotechnology Inc. 2018). Laboratory test reports were supplied to all study subjects. Statistical analysis was done using the paired *t* test for parametric data, the Wilcoxon test for non-parametric data, and a chisquare test for qualitative data. *P* value less than 0.05 was considered statistically significant. Statistical analysis was done using Excel 2013 and STATA 16.

The erythrocyte sedimentation rate was higher among the general and demographic parameters, and hemoglobin was lower in RA compared to the non-RA group. Plasma malondialdehyde and superoxide dismutase levels in both groups were measured as the parameters of oxidative stress, which showed no significant differences (**TABLE 1**).

HIGHLIGHTS

1. Age and sex-matched patients with or without rheumatoid arthritis recruited with a tertiary hospital were compared.
2. No significant changes were observed between the two groups in the measured oxidative stress defined by malondialdehyde and superoxide dismutase.

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Table 1 Plasma malondialdehyde and superoxide dismutase in patients with and without rheumatoid arthritis (RA)

Variables		Non-RA (n=30)	RA (n=30)	*P**
Age (years)	-	42.9 (11.2)	46.6 (10.1)	0.18
Body mass index (kg/m^2)	-	23.6 (3.2)	23.3 (3.2)	0.72
Sex**	-	23 (76.7)	23 (76.7)	0.99
Diabetes mellitus**	-	3 (10.0)	4 (13.0)	0.69
Hypertension**	-	3 (10.0)	5 (17.0)	0.45
Erythrocyte sedimentation rate (mm in 1st hour)	-	20.8 (18.2)	41.2 (29.6)	0.003
Hemoglobin (g/dL)	-	12.8 (1.6)	11.5 (1.3)	0.001
Malondialdehyde and SOD levels				
Age group				
≥55 years	Malondialdehyde	859.2 (197.9)	858.2 (422.4)	0.44
	Superoxide dismutase	73.8 (24.2)	57.2 (15.4)	0.14
<55 years	Malondialdehyde	990.5 (687.0)	1245.2 (1119.3)	0.46
	Superoxide dismutase	62.3 (13.7)	65.2 (10.7)	0.44
Sex				
Female	Malondialdehyde	1063.2 (682.1)	1146.6 (1023.0)	0.93
	Superoxide dismutase	61.6 (12.9)	61.8 (7.7)	0.95
Male	Malondialdehyde	658.0 (270.6)	1071.8 (853.6)	0.46
	Superoxide dismutase	72.8 (22.6)	66.0 (23.1)	0.58
Hypertension status				
Hypertensive	Malondialdehyde	963.2 (145.4)	1208.0 (1089.6)	0.79
	Superoxide dismutase	78.0 (19.2)	63.9 (8.9)	0.19
Normotensive	Malondialdehyde	969.3 (665.4)	1113.3 (971.3)	0.49
	Superoxide dismutase	62.7 (15.3)	62.5 (13.3)	0.97
Diabetes status				
Diabetic	Malondialdehyde	701.7 (221.0)	928.8 (227.6)	0.23
	Superoxide dismutase	78.7 (23.5)	60.3 (4.5)	0.25
Nondiabetic	Malondialdehyde	1009.7 (665.7)	1151.4 (1022.6)	0.89
	Superoxide dismutase	62.0 (13.9)	63.01 (13.18	0.78
Overall	Malondialdehyde	968.6 (631.2)	1129.1 (972.5)	0.66
	Superoxide dismutase	64.2 (16.0)	62.7 (12.6)	0.70

*Paired *t* test for parametric data, Wilcoxon test for non-parametric data, and chi-square test for qualitative data.
**Number (%); all others are mean (standard deviation).

In several studies, plasma malondialdehyde was significantly higher in patients with RA, while others found no difference.[3, 4] Higher plasma malondialdehyde levels in RA patients reported in those studies might be related to the severity of RA. A study revealed higher malondialdehyde levels in synovial fluid while serum malondialdehyde level was normal.[3] Some investigators found no change in plasma superoxide dismutase.[5] Several studies found a high level of superoxide dismutase[6] in patients with RA, whereas others found it to be low.[4] Further study may be conducted to overcome the limitations of the present study by collecting samples from synovial fluid or tissue rather than plasma during the active stage of the disease.

In conclusion, we did not find any statistically significant difference in plasma malondialdehyde or plasma superoxide dismutase levels between patients with or without RA. However, this finding should be cautiously interpreted because our finding is based on a small number of non-representative sample. Future studies using synovial fluid and other body tissue might provide more dependable results.

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Author contributions

Conception and design: SC, SS. *Acquisition, analysis, and interpretation of data:* SC. *Manuscript drafting and revising it critically:* SC, SS, SB. *Approval of the final version of manuscript:* SC, SS, SB. *Guarantor of accuracy and integrity of the work:* SB.

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Conflict of interest

We declare no conflict of interest.

Ethical approval

The study involves human subjects which was approved by the Institutional Review Board, BSMMU (Memo no. BSMMU/2020/9949 date: 15-11-2020).

Data sharing

The data that support the findings of this study are available on request from the corresponding author.

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