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RHEUMATOID ARTHRITIS;

IS RAISED SERUM MALONDIALDEHYDE IS AN INDICATOR FOR OXIDATIVE STRESS IN EARLY RHEUMATOID ARTHRITIS.

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ABSTRACT… Objectives: Objective of our study is to measure the concentration and role of Malondialdehyde in determining the oxidative stress in rheumatoid arthritis patients in comparison with healthy individuals. **Study Design:** Cross sectional study. **Setting:** Department of physiology Gujranwala Medical College and Shalamar Medical College, Lahore. **Period:** From October 2016 to October 2017. **Methodology:** 180 patients of age 49 to 70 years of either gender. The approval for conducting experimental study was taken from ethical committee and consent information was taken from the patient on prescribed Performa. Data was analyzed on SPSS Version 23 related to study. Continuous variables were presented as mean and standard deviation like age and serum MDA concentration.Categorical variables were presented as numbers and percentages like gender. Post operative chi square test was applied and p- value less than or equal to 0.05 was considered as significant. **Results:** Total 180 person (n=180) of either gender were included in this study. The study group was divided into two equal groups. Group A (RA group) consists of 90 patients (n=90) based on clinically and laboratory based criteria while group B (control group) consists of 90 (n=90) normal healthy individuals. The serum MDA levels in the RA patients were 3.97±1.03 nmoles/ml and it was 1.59±0.32 nmoles/ml in control patients. The difference was statistically significant (t=20.87, p=0.001). **Conclusion:** The observations of our study showed statistically significant raised serum Malondialdehyde level as compared to control group which shows that raised serum MDA is an indicator of oxidative stress in rheumatoid arthritis patients.

Key words: Malondialdehyde, Rheumatoid Arthritis, Lipid Per Oxidation, Free Radicals.

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INTRODUCTION

An inflammatory disease Rheumatoid Arthritis in particular has capability of continuous destruction of synovial joints. This condition also known as synovitis which may include deterioration of bones and cartilage and some others are systemic like pulmonary, cardiovascular, psychological and skeletal system abnormalities. Prevalence of rheumatoid arthritis reported as 1% in literature worldwide.[1]

Malondialdehyde (MDA) is a main contributing factor of DNA mutation in human and bacterial cells. Three types of mutations G→T, A→ G, and C→ T were found in base of cells of Escherichia coli, Salmonella typhimurium and also in some rats. It is produces as a result of lipid peroxidation and also from biosynthesis of prostaglandins, similar modifications were observed in human cells.[2]

Cytokines and T cells in combination with oxygen radicals and hydrogen peroxide plays major role in progressive activity of macrophages and enhancement of Rheumatoid Arthritis. Nitrogen and oxygen species have both types of effects beneficial and harmful.[3] Increased level of Malondialdehyde (oxidative stress) is a stage when reactive nitrogen and oxygen reaches to a damaging range and harm the cells and other biological body markers. When body's mechanism of antioxidants and oxidative stress become imbalance it can cause serious autoimmune diseases like Rheumatoid Arthritis.[4] Oxygen species in reactive form plays an important role in RA, main attack of these reactive

oxygen molecules is the unsaturated fatty acids. They damage nucleic acid, connective tissue and lipids of cell membrane, as a result of these damaging free radicals and their resultant products can cause inflammation by realizing mediators.[5] In synovial joints, synovial fluids have chemo attractant property. This property leads to the anaerobic glycolysis, enhancement of oxygen consumption and generation of hydroxyl, hypochloric radicals and superoxide. Among all these components neutrophils are found to be active in synovial fluid and cause erosion when rheumatoid arthritis develops.[6]

In lipid peroxidation malondialdehyde is an important factor and hallmark in the diagnosis of rheumatoid arthritis.[7] In recent studies it has been observed that early management of malondialdehyde reduces and delay the incidence of rheumatoid arthritis. In another study it has been observed that a significant increase in malondialdehyde level was found in serum of rheumatoid arthritis patients with p value was 0.0001 which is significant. Therefore, present study was carried out to determine the level of serum molondialdehyde in rheumatoid arthritis patients in comparison with normal healthy individuals.[9] This study will be a new gate towards modern health care and a local reference for diagnosis of rheumatoid arthritis which is helpful for clinicians. This study will develop a research related mindset in medical professionals of our region.

METHODOLOGY

This cross sectional study was conducted on 180 persons aged 49 to 70 years of either gender. In the department of Physiology Gujranwala Medical College and Shalamar Medical College, Lahore from October 2016 to October 2017. All persons were divided into two equal groups (90 patients in each group) as group A containing 90 arthritis based patients and Group B containing 90 healthy control persons. Non probability consecutive sampling technique was used. Sample size was calculated by using openepi.com an online source for sample size calculation by using confidence interval 95%, power of study 80% and P1 (concentration of MDAin RA group) 3.81±1.0 nmol/ml and P2 (concentration of MDA in healthy controls 1.72±0.44 nmol/ml. Complete physical examination, routine laboratory and radiological investigations were done. Rheumatoid arthritis was confirmed by X ray, C reactive protein, antinuclear antibody and rheumatoid arthritis factor. Patients of normal healthy diet, no history of nutritional supplement and post and pre menopausal women were included in the study. Patients with known history of diabetes, hypertension, smokers, alcoholic, history of anti inflammatory drugs and any trauma to joint were excluded from the study. With all antiseptic measures 5 ml blood was drawn from anticubital vein and sent to laboratory for laboratory investigation. Sampling tube was opened with care to avoid hemolysis. Blood was allowed to clot at room temperature for some time than serum was drawn after centrifugation (centrifugation was done at 3000 rpm for 15-20 minutes in morning shift. Hemolytic samples were discarded. Thiobarbituric acid assay test was used to estimate MDA concentration described by Buege and Aust (1978).[22] UV-VIS Spectrophotometer was used to calculate optical density. Thiobarbituric acid assay method measures Malondialdehyde by measuring aldehyde products of lipid peroxide. Exact mechanism behind this procedure is reaction of two molecules of thiobarbituric acid and one molecule of Malondialdehyde to make MDA-TBA red product which can be measured at 535 nm.

SPSS version 23 was used to analyze data related to study. Continuous variables were presented as mean and standard deviation like age and serum MDA concentration.Categorical variables were presented as numbers and percentages like gender. Post operative chi square test was applied and p value less than or equal to 0.05 was considered as significant.

RESULTS

Overall, there were 100% (n=180) patients were included, in this study. The study group was further divided into two equal groups, 50% (n=90) in each, i.e. Rheumatoid arthritis (RA) group and control group. The Mean±S.D age of RA patients was 54.61±4.61 years. While, the Mean±S.D age

of the control patients was 50.0±4.23 years. The difference was statistically significant (t=6.98, p=0.000). Gender distribution, in RA patients, was observed as 58.9% (n=53) in case of males and 41.1% (n=37) in females. When compared with control patients, 48.9% (n=44) as males and 51.1% (n=46) as females. The difference was statistically insignificant (χ^2 =1.81, p=0.178) (Table-I).

The serum MDA levels in the RA patients were 3.97±1.03 nmoles/ml and it was 1.59±0.32 nmol/ml in control patients. The difference was statistically significant (t=20.87, p=0.000). (Table-II).

DISCUSSION

Rheumatoid arthritis may be due to increased level of oxidative stress and serum MDA. After this continuous increase in MDA, chain reaction starts which gives continuous free radicals for continuation and new cycle of per oxidation. This whole cycle produced a new mixture of MDA. In many studies, MDA level was found to be raised in rheumatoid arthritis patients as compared to normal adults.[10]

In our study it has been observed that in RA patients there were 58.9% (n=53) as males and 41.1% (n=37) as females. So as compared to females male suffers more with RA. A similar study was conducted on Indian population in 2016 and reported that RA was mostly found in female patients.[8] In his study 16 male were diagnosed with RA and 34 female. Finding of this study shows that RA was common in female as compared to male population in India. These results are against our findings. In another study similar results were reported that RA was mostly diagnosed in female subjects as compared to male and the main contributing factor is increased malondialdehyde level in serum. Results of this study are also against our results and in favor of study conducted by Vyas et al (2016).[8] Post menupausal arthritis changes in female patients were also assessed in some studies but that is contributing factor of old age female. Malondialdehyde was found in all age groups.

In our study in RA patients serum MDA found to be increased when compared with controls. serum MDA levels in the RA patients were 3.97±1.03 nmoles/ml and it was 1.59±0.32 nmol/ml in control patients. The difference was statistically significant (t=20.87, p=0.000). Our results are similar to the study conducted by Gambhir et al[11] in 1997 who found increased level MDA in serum of rheumatoid arthritis patients as compared to healthy controls, p<0.001.

Similar studies were conducted by Mane et al[12] in 1999 and Vyas et al[8] in 2016 and reported increased level of MDA in serum of rheumatoid arthritis patients. This increased serum MDA due to increased production of free radicals and oxidative stress in rheumatoid arthritis patients. Result of these two studies are identical to our findings.

Moti[13] and Jaswalet al[14] also conducted similar studies and reported that free radical production and peroxidation was found in patients of rheumatoid arthritis and osteoarthritis patients. These studies were also in favor of our findings. A study by Karatas et al[15] also supports our findings.

Characteristics	RA* (n=90)	control (n=90)	Test of Sig.
Age	54.61±4.61 years	50.0±4.23 years	t=6.98, p=0.000
Gender	M=58.9%, F=41.1%	M=48.9%, F=51.1%	χ^2 =1.81, p=0.178

Table-I. Demographic characteristics of rheumatoid arthritis and control patients

Mean Serum MDA Concentration	RA* (n=90)	Control (n=90)	Test of Sig.
Mean±S.D	3.97±1.03 nmoles/ml	1.59±0.32 nmol/ml	t=20.87, p=0.000

Table-II. Mean serum malondialdehyde concentration (nmoles/ml) in Rheumatoid arthritis patients with that of controls

Similarly studies conducted by Paliwal et al[16] and Maneesh et al[17] and reported similar results to our study. They found increased serum enzymatic antioxidant marker and lipid MDA as compare to healthy controls P< 0.05. Results of these studies were significant and comparable to our results. Another similar study was conducted by El-barbaryet al[18] and reported similar finding.

In our study we found that serum Malondialdehyde level was increased in patients of rheumatoid arthritis, similar results were reported by Lunec et al in his study, he revealed that serum uric acid concentration found to be increased in serum and synovial fluid of RA patients.[19] Another study was conducted by Gambriz et al in 1997on topic of serum uric acid level in RA patients and reported that increase in serum uric acid concentration are the cause of RA specifically in aged patients.[20] Another similar study was conducted by Chaturvedi et al 1990 and reported similar finding that serum uric acid was increased in RA patient's blood. Findings of these studies are comparable with our findings and goes in favor of our results.[21]

CONCLUSION

The observations of our study showed statistically significant raised serum Malondialdehyde level as compared to control group which shows that raised serum MDA is an indicator of oxidative stress in rheumatoid arthritis patients.

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If you love your **cage** no one can set you **free**.

"Unknown"

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Khadija Kiran	Conceived idea, study design.	
2	Uzma Jamil	Data collection, Literature review.	
3	Amtul Huda Sobhi	Manuscript writing, data analysis.	
4	Zuhair Bhatti	Literature review, Proof reading	