International Journal of Sciences & Applied Research

www.ijsar.in

Study of lipid peroxidation (MDA) and antioxidant glutathione (GSH) level in the serum of RA

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Abstract
Rheumatoid Arthritis (RA) is one of the common autoimmune diseases with unknown etiology that its prevalence ratio in females to males is 3:1. It has been suggested that serum antioxidant levels is reduced and lipid peroxidation is increased due to oxidative stress. The aim of this study was to estimate levels of Malondialdehyde (the marker of lipid Peroxidation) & Reduced Glutathione (Nonenzymatic antioxidant marker) in serum of rheumatoid arthritis patients & compare them with the levels in normal healthy controls.A study was performed at the Department of biochemistry at SP medical college, Bikaner, Rajasthan. In 50 patients of rheumatoid arthritis serum levels of Non enzymatic Antioxidant & lipid Peroxidation marker were estimated by UV-VIS spectrophotometry. Fifty healthy controls were also included in the study & serum levels of same parameter also measured in them also. Serum level of Reduced Glutathione was significantly lower in the patients than in the controls. ($P<0.0001$). The serum Lipid Peroxidation marker (MDA) level was significantly increased in the patients than in the controls ($P<0.0001$). The increased oxidative stress in terms of lipid Peroxidation marker (MDA) in the rheumatoid arthritis patients is evidenced by decreased serum levels of non-enzymatic (GSH) antioxidant.

Keywords: Rheumatoid arthritis (RA), Reduced Glutathione (GSH), Malondialdehyde (MDA), Lipid Peroxidation

Introduction

Rheumatoid Arthritis (RA) is a heterogeneous disease with spectrum of clinical severity ranging from mild arthritis to a crippling joints disorder with internal organ involvement. Clinical disease progression in RA is usually monitored by standard clinical, laboratory and functional indices, whereas serial x-rays of hands and feet assess structural damage.[1]

RA has direct connection with other chronic diseases like cardiovascular diseases that are the most important problems of public health in community. Early identification of patients with aggressive destructive disease is important, not only for prognostic, but also for therapeutic reasons.[2]

At the sites of inflammation of joint increased free radical activity is associated with activation of neutrophils, phagocytosis by macrophages, which involve respiratory bursts phenomenon& uncoupling of variety of cellular redox systems. These process lead to ultimately increased peroxidation of

unsaturated lipids of the membrane. Lipid Peroxidation mediated by free radicals is considered to be the major mechanism of cell membrane destruction & cell damage.

Antioxidants are compounds that dispose, scavenge, & suppress the formation of free radicals or oppose their actions. This study evaluates the association between lipid Peroxidation & non-enzymatic antioxidant marker in rheumatoid arthritis Patients. To the best of our knowledge, only very few studies have been performed with respect to the estimation of the serum non-enzymatic antioxidant levels in patient with rheumatoid arthritis & their role in prevention & treatment of rheumatoid arthritis. In the light of this explanation, the present study was undertaken to determine the levels of the non-enzymatic antioxidant (GSH) in the serum.

Materials and methods

The present study was conducted on 50 healthy controls and 50 clinically established rheumatoid arthritis patients attending the Out Patient Department of Rheumatology, PBM hospital affiliated to SP Medical College, Bikaner. Serum MDA and GSH level was measured by UV-VIS spectrophotometer. A thorough physical examination was carried out on all the patients. Routine hematological & radiological investigation was also done. 50 cases selected from Rheumatology diagnosed by Rheumatologist. The presence of RA in patients was diagnosed by carrying out X- ray analysis of joint destruction as well as RF, C-reactive protein, & antinuclear antibody test.

Inclusion Criteria: Subjects with normal nutritional habits without supplementing with any vitamins during the last three months included in the study.

Exclusion Criteria: None of these subjects were alcoholic or chronic smoker & none of them suffered from any systemic diseases like hypertension, diabetes, not having any history of trauma to joints & also subject's history of receiving any anti-inflammatory drugs in the three months were excluded from the study.

MDA concentration will be estimated as reactive substances by a thiobarbituric acid assay method described by Buege and Aust (1978).[3] The reduced glutathione was estimated by kit method.

Results

The mean serum MDA concentration was found to be increased to 3.81±1.0 nmoles/ml with a range of 1.14-5.94 n moles/ml in Rheumatoid Arthritis patients. The increase level of MDA in RA patients was statistically highly significant as compared to that of normal control group 1.71±0.45 nmoles/ml, while it ranged from 0.64-2.56 nmoles/ml as evident by P-value (P<0.0001)

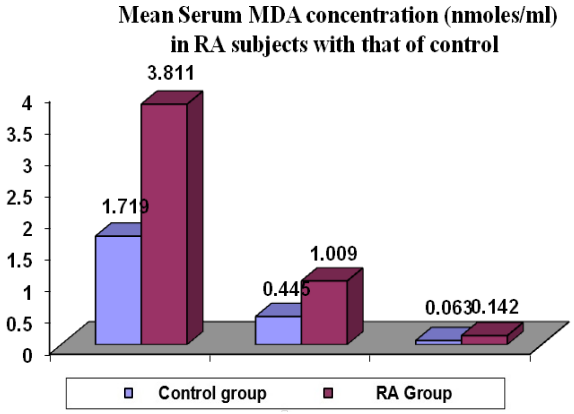
The results of present study of MDA concentration was similar to results obtained by previous studies which suggested that serum MDA level in RA patients increases significantly. As reported by Lunec et at (1981)[4], Gambhir et al (1997)[5], Chaturvedi et al (1999)[6], Shivani et al (2003)[7].

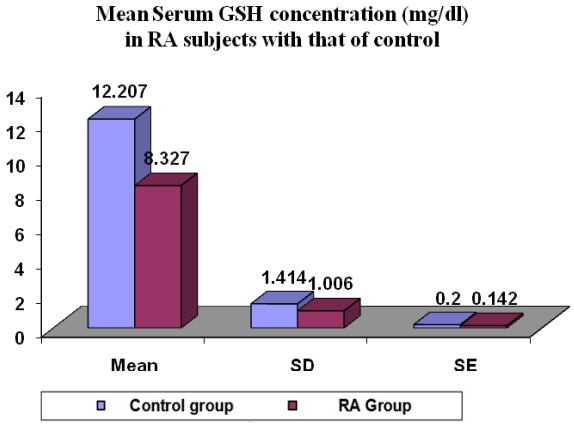
The mean serum Glutathione concentration was found to be decreased to 8.33±1.01 mg/dl with a range of 6.34-1089 mg/dl in rheumatoid Arthritis. The decrease level of serum glutathione in RA was statistically highly significant as compared to that of normal control group 12.21±1.41 mg/dl with a range of 9.21±15.21 mg/dl as it evident by P-value (P<0.0001).

The results of present study of serum Glutathione concentration was similar to results obtained by previous studies which suggested that serum Glutathione level in Rheumatoid Arthritis (RA) patients decreases significantly as reported by Hassan et al (2001)[8], Kamanli et al (2004)[9], Vijay et al (2006)[10], Palanisamy et al (2009)[11], Agnieszka et al (2012)[12].

Comparison of mean values of blood parameters in normal control subjects with Rheumatoid arthritis (RA)

Blood Parameters	*Normal Control subjects (n=50)*		*Rheumatoid Arthritis Patients (RA) (n=50)*		*Significant*	
	Mean ± S.D.	**S.E.**	**Mean ± S.D.**	**S.E.**	**t**	**P**
Malondialdehyde (MDA) nmol/ml	1.719 ± 0.445	0.063	3.811±1.009	0.142	13.413	**0.0001 HS*** **
Reduced Glutathione (GSH) mg/dl	12.207±1.414	0.200	8.327±1.006	0.142	15.804	**0.0001 HS*** **Highly significant





Discussion and conclusion

In this study, a highly significant correlation was observed when serum MDA and GSH level of RA patients was compared with healthy controls. The results of this study were concordant with Kartas et al (2003)[13]andAmal Mohammad et al (2011).[14] The statistically significant increase in serum MDA level in RA patients might be due to increased generation of reactive oxygen species (ROS) due to the excessive oxidative damage generated in these patients.

The decrease in serum GSH level might be due to various oxygen radical stresses have been shown to results in GSSG formation short term depletion of GSH. Reduced glutathione is also capable of directly scavenging radicals and peroxides by being oxidized to either GSSG or to a mixed disulphide, thereby preventing cell membrane lipid peroxidation and subsequent deleterious effects of cellular functions.

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