Research Article

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OXIDATIVE STRESS AND ROLE OF THIOL IN LEPROSY

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ABSTRACT:

Leprosy is a disease of great antiquity & it still continuous to be a significant health problem in few countries including India. Leprosy is a chronic infectious disease caused by mycobacterium leprae.Of the various mechanism that influences the pathogenesis of leprosy ,oxidative stress is important which occurs due to derangement in the balance between ROS and natural antioxidant.Considering this the study was planned to observe the status of oxidative stress in terms of lipid peroxidation and thiol as antioxidant in leprosy.In present study 50 leprosy patient &50 age and sex matched healthy controls were included.Out of 50 leprosy patient 34 were multibacillary(MB) leprosy patients and16 were paucibacillary(PB)leprosy patients. The level of Malondialdehyde as a marker of lipid peroxidation was found to be significantly increased in leprosy patients than controls. Again the level Malondialdehyde was found to be significantly increasd in multibacillary leprosy patients than paucibacillary leprosy patients.The level of thiolwas found to be significantly decreased in leprosy patients than controls. Again the level thiol was found to be significantly decreasd in multibacillary leprosy patients than paucibacillary leprosy patientsThe negative correlation among Malondialdehyde and thiol was observed among patients.Thus, increaseof lipid peroxidation and decrease in thiol leads protein modifications in leprosy which may be responsible for disease progression.

KEYWORDS:

Leprosy, Malondialdehyde(MDA)Multibacillary(MB),paucibacillary(PB) Thiol.

INTRODUCTION

Leprosy is a chronic infectious disease caused by mycobacterium leprae[1]. M.leprae is an obligatory intracellular parasite with affinity for the cells of Schwann and reticuloendothelial system mainly macrophages. The defence mechanism has primordial participation of macrophages, lymphocytes and its cytokines, regulating the production, release & modulation of diverse & important cellular immunity reactions[2].The infected foamy macrophages in skin and nerve show increased phagocytosis, enzyme activity and oxygen consumption known as respiratory burst[3].Burst of respiratory activity leads to production of a variety of molecules and free radicals called reactive oxygen species (ROS) such as superoxide anion, hydrogen peroxide, hydroxyl radicals etc[4,5].These ROS can damage lipids ,proteins and nucleic acids. Extensive damage can lead to death of the cell [4,5].The prime targets of peroxidation by ROS are the polyunsaturated fatty acids (PUFA) in membrane lipids. PUFA is degraded by free radicals to form malondialdehyde (MDA)[4].MDA in serum serves as a marker of cellular damage due to free radicals[4,5,6].Such ROS plays a significant role in infection with mycobacterium leprae in leprosy.

Thiols are the organic compounds that contain a sulphydryl group. Among all antioxidants that are available in the body, thiols constitute the major portion of total body antioxidants and they play a significant role in defence against ROS. Conversion of-SH groups into disulphides and other oxidized species is one of the earliest observable events during the radical mediated oxidation of proteins. The redox status of plasma thiols can be a diagnostic indicator of different pathological states [7,8].Oxidative stress(OS)is an expression used to

describe various deleterious processes resulting from an imbalance between free radical generating and scavenging systems.OS leads to metabolic impairment and cell death. It occurs if ROS are not scavenged by antioxidant [4].Considering this, the study was planned to observe the status of oxidative stress in patients with leprosy.

MATERIAL AND METHODS

The Present study was carried out in department of biochemistry, Dr.V.M.Govt. Medical college, Solapurin collaboration with Shree Chhatrpati Shivaji Maharaj general hospital Solapur. (Maharasthra). The protocol was approved by ethical committee of institute. The consent form was obtained from patients. A total of 100 individuals were included in this study .out of that 50 are clinically diagnosed leprosy patients and 50 healthy controls. The persons having disorders associated with heart, lung, kidney, other pivotal organs were excluded from the study. All the patients were comprised of clinically diagnosed leprosy patients of age group 21-60 years. Diagnosis and classification of leprosy was done by skin specialist as per WHO formula. The venous blood was collected from all the subjects under aseptic condition by venipuncture using 5 ml sterile syringe. Serum was obtained from this, and this serum was used for the estimation of Malondialdehyde (MDA) and thiol. The serum Malondialdehyde (MDA) was determined by Kei Satoh method[9], thiol by Habeeb method[10].

All d values of biochemical parameters in leprosy patients as well as in healthy controls were expressed as mean ± SD .All parameters in study groups were statistically compared with those estimated in controls and within the groups by using Z test and Tukeys test.Correlations between the variables were estimated by pearsons correlation coefficient. The difference was considered significant, when the $p<0.05$.

RESULTS

The present study was aimed to study the biochemical parameters, Malondialdehyde as a marker of lipid peroxidation in leprosy. Present study shows that there is statistically significant increase (P<**0.01**) in the level of Malondialdehyde (**Figure 1**) in paucibacillary as well as multibacillary leprosy patients when compared to controls. Furthermore, Malondialdehyde levels in MB leprosy patients are significantly higher (P<**0.01**), than in PB leprosy patients. Present study shows that there is statistically significant decrease (P<**0.01**) in the level of thiol (**Figure 2**) in paucibacillary as well as multibacillary leprosy patients when compared to controls. Furthermore, thiol levels in MB leprosy patients are significantly decreased (P<**0.01**), than in PB leprosy patients. A Negative correlation was observed between MDA and thiol in MB and PB leprosy patients. The results are depicted in **Table No.1 and 2**.

Figure 1: Indicates serum Malondialdehyde (MDA) level in healthy controls and patients with PB and MB Leprosy.

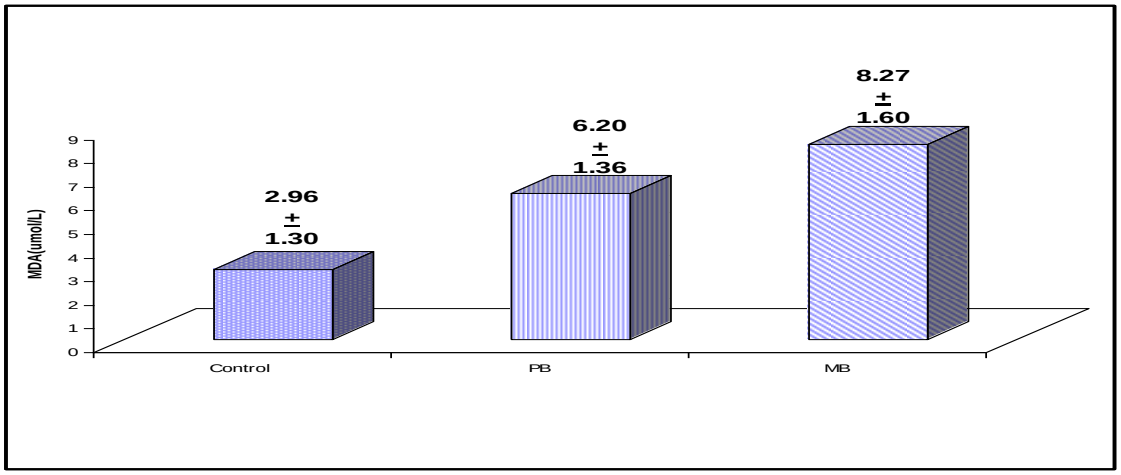

Figure 2: Shows serum Thiol level in healthy controls and patients with PB and MB Leprosy.

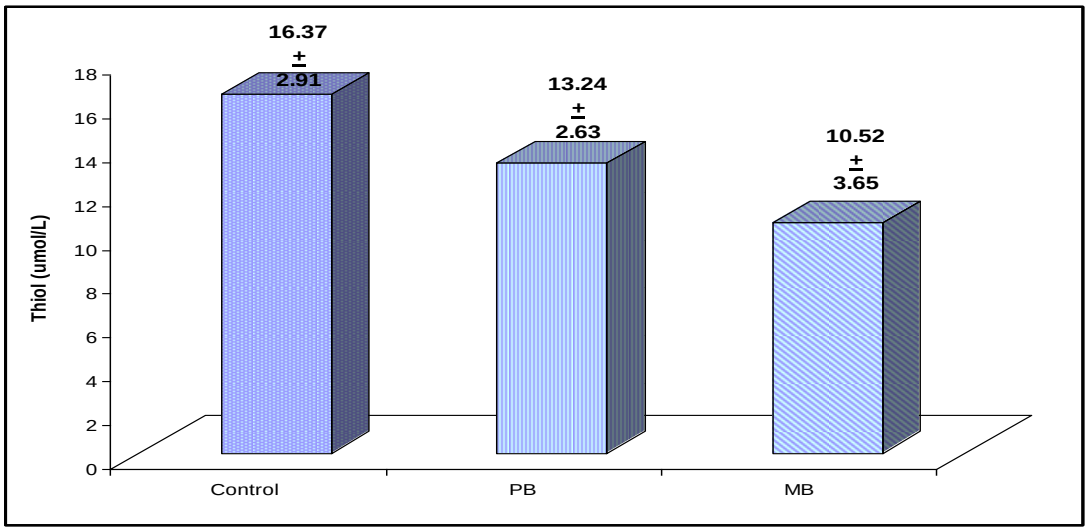

Table 1: Correlation among Malondialdehyde and thiol in MB Leprosy patients

	MDA
Thiol	r = -0.907

Table 2: Correlation among Malondialdehyde and thiol in PB Leprosy patients

	MDA
Thiol	r = -0.984

DISCUSSION

In recent years the phenomenon of lipid peroxidation has attracted considerable attention in several pathologic conditions. The major defence against microbial killing by macrophages system.Microbial killing by macrophages is associated with a burst of respiratory activity that leads to production of ROS. The primetargets of peroxidation by ROS are the polyunsaturated fatty acids (PUFA) in membrane lipids. PUFA is degraded by free radicals to form malondialdehyde (MDA)[4,6].MDA in serum serves as a marker of cellular damage due to free radicals[4,6].Since MDA serves as an index of lipid peroxidation, it was estimated in leprosy patients to estimate the extent of lipid peroxidation.MDA levels in both PB and MB leprosy patients were significantly elevated compared to those in normal controls.This indicates that increased lipid peroxidation due to free radical mediated injury occurs in leprosy patients.The present study shows significantly higher MDA levels from PB to MB. In PB leprosy there is defective monocyte-macrophage function.The macrophages in PB leprosy shows normal phagocytosis ,but they are unable to kill the M.leprae. due to inadequate superoxide production[4]. In MB leprosy the source of ROS could be some other subpopulation of phagocytes in which normal respiratory burst occurs like immunologically activated macrophages,neutrophilsand other sources.

According to **S.B.Trimbakem et.al.[4], V.R. Bhadwat,et.al[3], Reddy Y.N. et.al.[11] ,. Balsubramanya Prasad C et.al[12], P. Jyothi et.al.[13]G. Ozanet.al.[14]**the MDA values increased from TT to LL, thus indicating increased trend in the mean values in leprosy patients, thus indicating increased lipid

peroxidation in leprosy particularly in LL. Our results are in accordance with above authors.

In present study we found that serum thiol is significantly decreased in leprosy patients when compared with healthy controls. Furthermore there is significant decrease in thiol is observed in MB when compared with PB leprosy patients.Thethiol groups are preferred target for NO attack to form s- nitrosithiol[15]. $NO^{\bullet}$ formation may have originated as a first line defense against invading microbial organisms including parasites, bacteria, viruses[16,17].Under physiological condtions, $NO^{\bullet}$ may react with thiol containing molecules such as glutathione (GSH) to form S-nitrosothiols[15]. S-nitrosothiols have been recognized to possess antimicrobial activity. These compounds have also been proposed to mediate $NO^{\bullet}$ transfer to outer membrane thiols in bacillus, which inhibits spoure outgrowth. Differences in stability and target response relative to $NO^{\bullet}$ lead credence to the suggestion that S-nitrosothiols are important physiologic redox forms of $NO^{\bullet}$. N-nitrosamine and S-nitrosothiols are formed by the addition of nitrosonium equivalent (NO^{+}) to amine and thiol respectively[17].As far as our knowledge no study would be done on thiol in leprosy.The $NO^{\bullet}$ attacks on thiol groups to form nitrothiols, Nitrothiol acts as $NO^{\bullet}$ carrier. Thus in leprosy increase in $NO^{\bullet}$ may increase nitrothiol formation .The bond formed between thiol and $NO^{\bullet}$ ($S–NO^{\bullet}$) is weak. Homolytic or heterolytic cleavage releases reactive nitrogen intermediates. The remaining free thiols reacts with other free thiol groups within same protein to form disulphides. Due to formation of disulfides the thiol level might be reduced.A negative correlation was observed between MDA and Thiol in MB and PB leprosy patients.This is clearly indicated that elevated levels of MDA decreases thiol levels. Thus, increased in oxidative stress is most likely to be due to inadequate scavenging of ROS due to decreased levels antioxidant defense such as thiols. This study confirms the presence of oxidative stress in leprosy which is maximum in MB leprosy which may be responsible for disease progression.

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