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*Original Research Article*

# Status of Lipid Peroxidation, Vitamin E and Catalase Activities and Their Association in Schizophrenia

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## ABSTRACT

Free radical mediated pathological processes may have a role in schizophrenia. Free radicals cause cell injury, when they are generated in excess or when the antioxidant defence is impaired. The exact pro-and antioxidant status in schizophrenic patients is still not clear. To add a new insight to the question, changes in the erythrocyte lipid peroxidation products (MDA), levels of plasma Vitamin E and activities of antioxidant enzymes like Catalase in erythrocytes were studied in 30 schizophrenic patients and 30 healthy subjects. The blood samples were collected and investigated for lipid peroxidation end product as Malondialdehyde and activity of antioxidant enzyme Catalase, level of Vitamin E in schizophrenic patients and healthy subjects. The level of Malondialdehyde was found to be significantly increased in patients than healthy controls; also a significant decrease in vitamin E in schizophrenic patients was seen as compared to controls. The difference in the activity of the CAT was not significant when compared between patients and controls. The results of our study have shown higher oxygen free radical production, evidenced by increased levels of MDA and decreased levels of Vitamin E which supports the oxidative stress in schizophrenic patients. Intensive oxidative stress and decreased antioxidants may contribute to the neuronal death and alter the information processing in schizophrenia. These findings also provide a theoretical basis for the development of novel therapeutic strategies, such as antioxidant supplementation. This may suggest the hope for the use of antioxidants in clinical trials to prevent and treat schizophrenic patients.

***Key words***: Malondialdehyde (MDA), Vitamin E, Catalase (CAT), Oxidative stress, Schizophrenia.

## INTRODUCTION

Schizophrenia is a common psychiatric disorder. It is the major mental disorder of the brain resulting from abnormalities that arises early in the life and disturbs normal development of brain. [(1)] The brain and nervous system are particularly prone to free radical damage since the membrane lipids are very rich in polyunsaturated fatty acids and areas of human brain are very rich in iron, which plays an essential role in generating free radical species. [(2,3)]

If the homeostasis between rate of formation of free radicals and the rate of

their neutralization of free radicals is not maintained, an oxidative stress occurs. [4]

The potential toxicity of free radicals is counter acted by a large number of cytoprotective enzymes and antioxidants that limit the damage.

One of the most important biological membrane functioning disturbances includes lipid peroxidation. Multiunsaturated fatty acids as well as their residues (parts of phospho and glycolipids) undergo peroxidation. Malondialdehyde (MDA) is a secondary lipid peroxidation end product and is specific marker of lipid peroxidation of membrane.

Lipid peroxidation may be initiated by $OH^{\cdot}$, $O_2^{-}$ or $OH_2^{\cdot}$ radicals. Final products of lipid oxidation include aldehydes especially Malondialdehyde (MDA), which diffuse to different cell parts, damaging protein - lipid membranes and which disturb vessel permeability and neuronal conduction.[5]

Lipid peroxidation and derived oxidized products are being intensively investigated because of their potential to cause injury and their pathogenic role in schizophrenia.

The human body has a complex antioxidant defence system that includes the antioxidant enzymes Superoxide dismutase, Catalase (CAT) which blocks the initiation of free radical chain reactions. Vitamin E is a major lipid soluble non enzymatic antioxidant and is most effective chain-breaking antioxidant within the cell membrane where it protects membrane fatty acids from lipid peroxidation. [6]

In the present study, the level of lipid peroxidation product (MDA), the activity of Catalase, Vitamin E level and their association were assessed in schizophrenia.

## MATERIALS AND METHODS

The present study was carried out in Department of Biochemistry Dr. V. M. Government Medical College, Solapur, in collaboration with Shree Chhatrapati Shivaji Maharaj General Hospital, Solapur, (Maharashtra). The protocol was approved by Ethical committee of the institute. The consent form was obtained from the relatives of patients. A total of 60 individuals were included in this study. Out of these, 30 were clinically diagnosed as schizophrenic patients.

The study subjects having disorders associated with heart, lung, liver, kidney and other pivotal organs were excluded from the study. Diagnosis of schizophrenia was made by Psychiatrists by using Diagnostic and statistical Manual of Mental Disorders (DSM-IV) classification (American Psychiatric Association, 1994.[7]

The venous blood samples were collected from the subjects under aseptic condition by venipuncture using 10ml sterile syringe and needle About 8ml of random blood was collected of which 3ml was poured into sterile vacutainer containing heparin for the estimation of CAT. Remaining blood was taken into sterile vacutainer for estimation of other parameters. Then the plasma and serum were separated by centrifugation at 3000 rpm for 5-10 minutes and unhemolyzed samples were taken for the assays. Plasma MDA level were determined by a Kei Satoh method.[8]The activity of Catalase by L. Goth Method,[9] plasma vitamin E by Frank et al.[10] All the values biochemical parameters of patients and controls were expressed as mean ± SD. All the biochemical parameters measured in study group subjects were

statistically compared with those estimated in control by using student "t" test. Correlations between the variables were estimated by Pearson's correlation coefficient. The difference was considered significant, when the $p<0.05$.

## RESULTS

The present study was aimed to study the biochemical parameters viz. Malondialdehyde (MDA), Catalase (CAT), and Vitamin E in the patients of schizophrenia and healthy controls. The levels of Lipid peroxidation end product MDA was increased significantly ($p<0.05$) in patients of schizophrenia when compared with healthy controls, while there was no significant ($p>0.05$) difference found in Catalase (CAT) in patients and controls. The level of Vitamin E was found to be significantly decreased in patients of schizophrenia than the healthy controls. The results are depicted in table no.1.The correlation between Serum CAT activity and vitamin E was studied with MDA. We found negative association between Serum CAT activity and MDA with r value of -0.780 and associated p value <0.01. Vitamin E activity was also negatively correlated with MDA in patients with r value of -0.945 and associated p value <0.01. The values are depicted in table no.2 and scatter diagrams are shown in figure 2 and 3.

Table No 1: Showing levels of serum Malondialdehyde (MDA), activity of Catalase(CAT) and Serum Vitamin E levels in healthy controls and schizophrenic patients.

| Biochemical Parameters | Healthy Controls (n=30) | Patients (n=30) |
|---|---|---|
| Serum MDA (nmol/dl) | 258.93±92.40 | 405.3±248.75* |
| Serum CAT(KU/L) | 368.65±209.20 | 391.68±243.66# |
| Serum vitamin E (mg/dl) | 1.02±0.42 | 0.27±0.19* |

* Highly significant
\# Non significant

Table No.2: Association of MDA with serum CAT activity and Vitamin E.

| Parameters | Malondialdehyde(MDA) | |
|---|---|---|
| | 'r' | P |
| Serum CAT activity | -0.780 | <0.01* |
| Serum Vitamin E | -0.945 | <0.01* |

* Statistically significant.

## DISCUSSION

The results indicate that there is increase in free radical generation and antioxidant defence is impaired in schizophrenic patients. Impaired antioxidant defence and increased lipid peroxidation have been reported in schizophrenic patients. [(11)] The free radicals play an important role in the genesis of structural and functional changes in neuronal membrane that could be responsible for the beginning or aggravation of the psychiatric disorders including schizophrenia. [(12)]

The brain and nervous system possess high potentials for the initiation of free radical reactions, which relative to other tissues, can cause more damage in the brain and nervous system due to insufficient antioxidant protection and existing intensive aerobic metabolism accompanies with oxygen radical production. [(13)]

In previous studies the activity of Catalase and Vitamin E level along with some free radicals were evaluated in different psychiatric disorders. They have found significant differences among free radical and antioxidant levels in patients than controls.

The results of present study indicate , there is increase in free radical generation and antioxidant defense is impaired in schizophrenic patients. The level of MDA was increased significantly, and Catalase activity was not differed statistically among patients and controls. Vitamin E level was significantly decreased in patients of schizophrenia when compared with healthy controls.

Our findings were consistent with those reported by Yao et.al.[(14)] H.Herken

et.al, [15] no any significant difference in catalase activity of schizophrenia of all types in drug free condition. Mahadik et.al [5] Li. Hui Chun et.al.[16] found decreased activity of Catalase in schizophrenic patients. Rukmini M.S. [17] found increased activity of catalase in schizophrenic patients. While low catalase activities had been reported by Shashikant Nikam et.al. [18] in Parkinson's disease. This discrepancy may be due to the different duration of the disease in different studies. Rukmini M.S., Bendicta D'souza et.al.[17],Birsen Ozyurt, Fikret et al [19], Meena Arvindakshan et. al. [20] showed significant increase in plasma MDA level in patients. , Our results support the findings of Dusica Pavlovic, Vensna Tamburic et. al, [3] they had shown that, the levels of MDA was increased in schizophrenic patients than the healthy controls. Our results also supported by Dadheech Gora et. al, [21] Surapaneni K. M. et.al. [22] observed significant decrease in levels of vitamin E in schizophrenic patients.

Rise in MDA could be due to increased generation of Reactive Oxygen Species (ROS), due to excessive oxidative damage generated in the schizophrenics. These oxygen species, in turn, can oxidise many other biomolecules, including membrane lipids. The lipid peroxides and free radicals may be important in the pathogenesis of schizophrenia.[4] MDA is responsible for membrane oxidative injury in schizophrenia, which is attributed to free radical formation that abstracts hydrogen atom from lipo-proteins, causing lipid peroxidation. The membrane phospholipids specifically PUFA are converted to MDA by lipid peroxidation render cellular membranes vulnerable to damage from free radical causing peroxidation. The damage induced by lipid peroxidation renders the cell unstable and therefore, compromises fluidity, permeability, signal transduction and causes receptor mitochondrial DNA and nuclear alterations. High density polyunsaturated fatty acid is quite sensitive to free radicals, increased lipid peroxidation reaction occurs and produces more lipid peroxides that damages the neuron membranes. [4,23,24,25]

Vitamin E is responsible for scavenging the free radicals and suppression of peroxidation in aqueous and lipid region of the cell. The decrease in the levels of these non-enzymatic antioxidant may be due to the increased turnover for preventing oxidative damage in these patients, suggesting an increased defense against oxidative damage in schizophrenic patients and decrease vitamin E level might also be due to increased consumption of vitamin E for free radical neutralization.

Also found negative correlation between MDA and Catalase may suggest that Catalase is involved in antioxidant defence system against free radicals. As well as between MDA and Vitamin E .The negative correlation of MDA with Catalase and Vitamin E in our findings show the effect of increased oxidative stress in schizophrenics leads to decreased antioxidants like vitamin E, Catalase and disturb their metabolism, and may contribute to neuronal death and alter the information processing in schizophrenia.

## CONCLUSION

So, the treatment with antioxidants in initial stages of the disease may be useful as secondary therapy to prevent the oxidative damage and deterioration of the neural tissues in schizophrenic patients. Further studies are needed to use antioxidants such as

Vitamin E, Catalase as secondary therapy, in addition to current drug therapy in schizophrenia.

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