

## To Estimate Serum Lipid Peroxide, Superoxide Dismutase, Glutathione Reductase, Zinc, Magnesium and Copper in Different Psychiatric Disorders

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### Abstract

**Background:** Health is considered to be wealth. All of us want to be healthy. However, where absence of illness is not healthy, a healthy person has a sound body. He is happy and contented. He has the ability to face difficulties, losses and frustrations. He is capable of living in harmony with others. Not only is he happy but is able to keep others happy. He sees that others are not put into trouble because of him; he has certain moral and spiritual values. Such a person who is physically, mentally, socially and spiritually alert can be considered to be healthy. The establishment of definite link between the variability of plasma or serum lipid peroxide levels and disease link arteriosclerosis, diabetes and heart ailment, has been largely responsible for an increased interest in these biochemical parameters. In the light of the above facts the present study was undertaken to evaluate the different biochemical parameters in the patients with psychiatric disorders

**Aim:** To estimate serum lipid peroxide, Superoxide dismutase, Glutathione Reductase, zinc, magnesium and copper in different Psychiatric disorders. To find out the biochemical changed occurs in Psychiatric disorders

**Material and Method:** The present study was carried out in the Department of psychiatry. A total of 150 subjects were enrolled for the study and were divided into 4 groups. They were selected from Psychiatric Ward. Consent was obtained from the attendants of the patients. The patients were randomly selected. To assess the serum lipid peroxide, Superoxide dismutase, Glutathione Reductase, zinc, magnesium and copper in different Psychiatric disorders. Groups are divided into following types: Group I: Normal patient Group II: Manic Depressive Psychosis, Group III: Schizophrenia, Group IV: Other Psychiatric Disorders

**Results:** In psychiatric disorders there were a significant decreased levels of zinc and significant increased levels of serum lipid peroxide. Therefore, there was a decreased level of superoxide dismutase in the patients suffering from psychiatric disorders. Serum zinc levels in schizophrenia were significantly lower than controls. There appears to be a deficiency state of zinc in the patients. Serum copper levels in schizophrenia were found to be elevated. This may not have direct relationship with the disorders. In psychiatric disorders serum levels of all the four trace elements were abnormal. Zinc, magnesium and copper 'V was lower than control. The lower levels of zinc, copper and magnesium appear to reflect an impaired ability of these patients to regulate copper, zinc and magnesium metabolism as a result of sub-optimal functioning of nervous and neuroendocrine system in these patients.

**Conclusion:** In psychiatric disorders serum levels of all the four trace elements were abnormal. Zinc, magnesium and copper 'V was lower than control. The lower levels of zinc, copper and magnesium appear to reflect an impaired ability of these patients to regulate copper, zinc and magnesium metabolism as a result of sub-optimal functioning of nervous and neuroendocrine system in these patients. Further, detail and controlled studies are required before any causal relationship is to be established with the alternation in the serum levels of these trace elements along with other parameters.

**Keywords:** Manic Depressive Psychosis, Schizophrenia, Psychiatric, Superoxide dismutase, Glutathione Reductase, zinc, magnesium.

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## Introduction

World Health Organization defines health as a state of complete physical, mental and social wellbeing and not merely absence of disease. Therefore, health is considered to be wealth. All of us want to be healthy. However, where absence of illness is not healthy, a healthy person has a sound body. He is happy and contented. He has the ability to face difficulties, losses and frustrations. He is capable of living in harmony with others. Not only is he happy but is able to keep others happy. He sees that others are not put into trouble because of him; he has certain moral and spiritual values. Such a person who is physically, mentally, socially and spritually alert can be considered to be healthy. [1]

Like the body the mind too can become ill. In mentally disturbed persons, sense of wellbeing and equilibrium are disturbed. Various functions like thinking, emotional behavior, memory, intelligence etc. get disturbed. Speech and behavior become abnormal. Ability to perform work satisfactorily is impaired. The development of psychiatric disorder or mental disorder depends upon an interaction between the predisposing and precipitating factors. Predisposing factors determine an individual's vulnerability to develop physhiatic disorders. Many of these factors operate right from early life. [2,3]

Some of the factors are: (a) Biological Factors: Heredity, constitution, Metabolic and biochemical abnormalities. Physical

defects (b) Psycho-social Factors: Personality, faulty parent child relationship. Psychological experiences in early years. Any Stress - Physical, Physiological and/or psychological exacerbates the tension and precipitates the various psychiatric disorders which may manifest a disturbances in Physiological, Psychological and social functioning. [4]

Psychiatric disorders have traditionally been classified into main groups: i) Organic ii) Functional. In the organic disorders a known physical etiology can be established, the symptoms resulting from coarse brain disease such as dementia from metabolic upset or circulating toxins as in acute confusional states. The functional disorders constitute large majorities of psychiatric illness where no such physical factors can be demonstrated. [5]

Diagnosis begins with the physical examination of the patient. The diagnosis in particular of phvsiatric or mental disorders is also arrived at by carrying out the physical tests which provide clues for a probable cause. The cause of most psychiatric disorders is unknown. The diagnosis of a mental illness or psychiatric disorder is arrived at by carrying out certain tests. [6]

It is a well-known fact that all tissues require constant supplies of oxygen and of oxidizable substrates. Under normal conditions brain metabolism is

characterized by an extremely high consumption of oxygen and an almost exclusive dependence on glucose as a source of energy. The mechanism of tissue injury has been a major thrust area for research for several years. It had been considered that most injuries were due to necrosis, anoxia or infarction. In the recent years another major mechanism of cell injury has been proposed - de novo generation free oxygen radicals which are produced during metabolism of all aerobic cells through activation of xanthine - xanthine oxidase system or glucose - glucose oxidase. Recent experimental studies have demonstrated that the free oxygen radicals may be important mediators of neutral injury, neutral damage. [7]

The establishment of definite link between the variability of plasma or serum lipid peroxide levels and disease link arteriosclerosis, diabetes and heart ailment, has been largely responsible for an increased interest in these biochemical parameters. In the light of the above facts the present study was undertaken to evaluate the following biochemical parameters in the patients with psychiatric disorders: i) Lipid Peroxide. ii) Glutathione Reductase. iii) Super Oxide Dismutase. iv) Serum Zinc levels. v) Serum Copper levels. vi) Serum Magnesium levels.

### Material and Methods

The present study was carried out in the Department of Psychiatry. The study was consisting of one hundred (100) patients with various psychiatric disorders and fifty (50) healthy individuals. Patients and normal individuals were included from both the sexes.

Healthy individuals were symptomless and did not exhibit any abnormality on clinical examination in the context of metabolic disorders and nutritional deficiencies. The diagnosis and classification of psychiatric disorder patients was done by the eminent

psychiatrists from the above mentioned hospitals.

There are different types of psychiatric illness. Some are severe and some are mild in nature. They are broadly classified into: a) Schizophrenia b) Manic depressive psychosis c) Organic psychosis. Other disorders like a) Epilepsy b) Down syndrome c) Senile dementia d) Alzheimer disease e) Neurosis, etc. Since the number of patients from other disorders and organic psychosis were limited, they are included in one group namely miscellaneous group. And therefore, for the present study patients were divided into three groups as under.

- Group I: Manic Depressive Psychosis
- Group II: Schizophrenia
- Group III: Other Psychiatric Disorders

### Sample Collection

Sample Collections: Patients were not allowed to take anything by mouth for 12 hours prior to collection of blood samples. Blood samples were drawn and dispensed slowly. Large bore needles were used to minimise haemolysis, for the same reason, the needle was removed before dispensing the whole blood into plastic tube during sampling. The blood was drawn in the morning and fasting state was taken into consideration. Each subject was prepared by cleaning the site with separate alcohol swabs. The 20 gauge stainless steel needle was attached to a 10 ml. syringe, 5 ml. of blood was slowly drawn into syringe. The needle was removed, and the blood was dispensed evenly stoppered plastic tube without any anticoagulant. The tubes were kept until clot retracts and then centrifuged approximately at 2000 rpm. For 10 minutes, within two hours of collection. The serum was separated into another stoppered plastic tube and stored at 4° C until tested.

### Trace Element

On these subjects' clinical diagnosis had already been made at the time of taking blood sample. Patients were seen by psychiatrists who gave a clinical

diagnosing using the criteria of the glossary to the international classification of disease. They were not apparently taking any medicines at the time of blood sampling.

### Methods:

- ✚ Lipid peroxidation can be standardized by the new colorimetric method by Kei Satoh.
- ✚ Catalase was assayed according to the method of Takahara et al., 1960.
- ✚ SOD was assayed by the method of Misra and Fridovich, 1972.
- ✚ The activity of glutathione reductase was determined by the method of Shrier et.al
- ✚ Williams H.L. et.al. utilized a non-precipitation technique, for the estimation of serum zinc
- ✚ Serum magnesium was determined by photoelectric colorimetric method using the Titan yellow method of Neill

and Neely. Total CK was analysed by semi auto analyser Micro lab 200 by UV kinetic IFCC method.

- ✚ Johnson D.J. et al. utilized the non-precipitation technique, with a sensitive chromogenic indicator 4 (2 pyridylazol) resorcinol, for the estimation of serum magnesium with colorimeter.

### Statistical Analysis:

Statistical evaluation was carried out using SPSS (Version 14.0) Data obtained from the study groups were compared by the parametric student's t test; correlation analysis between variables were made by Pearson test. All the results were expressed as means with their standard deviation (mean  $\pm$  SD). Statistical analysis was also performed by using standard deviation and ANOVA.

### Result:

**Table 1: Comparison of plasma Glutathione reductase, SOD, Lipid Peroxide in Manic Depressive Psychosis, Schizophrenia and Other Psychiatric Disorders and normal patients**

Groups	Glutathione reductase (mg %)	SOD (Units/mgm of Hb)	Lipid Peroxide (n-mole)
Group I	39.21 $\pm$ 8.52	38.48 $\pm$ 7.10	3.63 $\pm$ 0.72
Group II	17.88 $\pm$ 9.31	35.74 $\pm$ 9.87	4.78 $\pm$ 0.80
Group III	16.84 $\pm$ 8.33	35.77 $\pm$ 11.28	4.55 $\pm$ 0.14
Group IV	15.93 $\pm$ 5.08	34.19 $\pm$ 8.88	4.44 $\pm$ 0.86

Lipid peroxide is significantly more in subjects with psychiatric disorder than in control. Serum superoxide dismutase is not significant in control and in subjects with psychiatric disorders. Serum glutathione reductase is significantly more in controls than in subjects with psychiatric disorders.

**Table 2: Comparison of plasma Zinc, Copper and Magnesium in Manic Depressive Psychosis, Schizophrenia and Other Psychiatric Disorders and normal patients.**

Groups	Zinc ( $\mu$ g %)	Copper ( $\mu$ g %)	Magnesium ( $\mu$ g/dl)
Group I	114.37 $\pm$ 26.03	116.56 $\pm$ 17.55	3.43 $\pm$ 0.35
Group II	96.47 $\pm$ 7.89	115.76 $\pm$ 24.59	3.28 $\pm$ 0.50
Group III	94.38 $\pm$ 17.41	163.64 $\pm$ 57.98	2.81 $\pm$ 0.57
Group IV	99.70 $\pm$ 15.43	122.7 $\pm$ 44.58	3.18 $\pm$ 0.49

Serum zinc is significantly more in controls than in subjects with psychiatric disorders. Serum copper is significantly more in subjects with psychiatric disorders group II

(Schizophrenia) than in Group I (MDP) and group III (Misc). Serum magnesium is significantly more in controls than in subjects with psychiatric disorders. Lipid

peroxide is significantly correlated with magnesium levels in Group II – SCH. Lipid peroxide is significantly correlated with magnesium levels. Group III – Miscellaneous. Lipid peroxide is significantly correlated with magnesium levels in Group III – Miscellaneous.

### Discussion

Despite of the vast amount of work done on the Psychiatric disorders, there are very few reports on the laboratory tests which could lead in diagnosing the psychiatric cases. "The red cell plays an important role and is responsible for oxygen transport of other metabolites from one organ to another and from tissues.

Lipid peroxidative chain reactions with subsequent disruption of both liposomal and cellular membranes may be induced by enzymatically generated free radical. [8] lipid peroxide is obviously more than anything that should be present in the hydrophobic interior of a biological membrane. Lipid peroxidation diminishes membrane fluidity, increase non-specific permeability to ions that may inactivate membrane bound enzymes. The most popular current theory to explain  $O_2$  toxicity is the so-called superoxide theory of  $O_2$  toxicity. There is much evidence consistent with the superoxide theory. In present study there is decrease in superoxide dismutase levels in all three groups, but lower levels are not significant. This non-significant decrease level in SOD may be probably due to the mild stress observed in the subjects with psychiatric disorders while such characteristic decrease is not observed in severe stress conditions, toxicity and others. [9]

The damage to red cells due to production of the free radicals occurs only if an abnormally increased oxidant stress exceeds the normal reducing capacity or due to structural defects in the red cells which render them susceptible to oxidant stress despite normal reducing power or a deficiency in the reducing capacity which is

unable to counteract the increased oxidant stress. [10]

Our study shows that there is a considerable amount of decrease in GSH. An increased lipid peroxidation leads to membrane damage causing depletion of GSH which is essential to maintain the membrane integrity. The corresponding enzyme Glutathione Reductase do not show any increase in activity. This shows that the toxic products are being detoxified possibly through another pathway, perhaps SOD seems to account for this. However, this decrease in our study is not sufficient to maintain a proper balance hence in the moderate increase in lipid peroxidation and depletion of GSH. [11]

Stern (1964) and Sobel (1988) [12] showed that the hypozincemia in person with Down syndrome could also be caused by intestinal malabsorption, malabsorption of calcium and vitamin A. Danford and Huber (1982) [13], Palmer and Ekvall (1978) [14] observed that the low level of serum zinc in pica behaviour of person with mental retardation. Pica is the most frequently observed eating dysfunction among mentally retarded persons. Zinc deficiency having reached a certain low level may induce an abnormal food habit in order to obtain zinc from other sources. Henkin et. al. (1975) [15] found that zinc deficiency may contribute to the causation of schizophrenic symptoms. In this context it is interesting to note that condition associated with zinc deficiency such as, pregnancy, post operative state, alcoholism, liver failure, porphyria and medication with steroids are all potential situations, where a schizophrenia like manifestation can occur.

Much - Peterson et.al. (1950) [16] and Horwitt et.al. (1957) reported that the serum copper concentration raised in schizophrenia disease. The serum oxidase activity has also been reported increase in this disease by Akerfeldt (1957) [17] Underwood (1911) [18] Williams H.L (1977) [19] found that the copper enzyme

cytochrome oxidase and tyrosinase regulate oxidative process in brain cell and formation of neurotransmitters. Copper deficiency caused a progressive neurodegeneration in male infant's with menck disease. A report by Stern and Lewis (1960) [20] that serum magnesium is elevated in 15% of children with Down syndrome and in 7% of other mentally retarded children could not be confirmed. M.Car.ce R.A. et.al. (1931) [21,22] suggested that high magnesium levels occur non-specifically in a number of diseases including neurological disorder.

### Conclusion:

In psychiatric disorders serum levels of all the four trace elements were abnormal. Zinc, magnesium and copper 'V' was lower than control. The lower levels of zinc, copper and magnesium appear to reflect an impaired ability of these patients to regulate copper, zinc and magnesium metabolism as a result of sub-optimal functioning of nervous and neuroendocrine system in these patients. Further, detail and controlled studies are required before any causal relationship is to be established with the alternation in the serum levels of these trace elements along with other parameters.

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