

## Original Research Article

# Study of malondialdehyde as an oxidative stress marker in schizophrenia

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### ABSTRACT

**Background:** Schizophrenia is characterized by distortions in thinking, perception, emotions, language, sense of self and behaviour. It has been demonstrated that free radical-mediated damage has an important role in the pathophysiology of schizophrenia. The present study was undertaken to study malondialdehyde as an oxidative stress marker in first episode and chronic schizophrenic patients.

**Methods:** 50 patients of first episode schizophrenia and 50 patients of chronic schizophrenia were included in the study. 50 numbers of age and sex matched healthy and apparently normal controls were also selected for study. Blood samples were drawn and analysed for malondialdehyde (MDA) from all participants.

**Results:** The study shows significant increase in plasma malondialdehyde (MDA) levels in both first episode schizophrenics and chronic schizophrenic patients as compared to controls. When we compared levels of these parameters in first episode schizophrenics and chronic schizophrenics, we did not find significant difference.

**Conclusions:** Findings in our study is suggesting that increase in the levels of plasma malondialdehyde (MDA) occurs due to increased lipid peroxidation in schizophrenics.

**Keywords:** MDA, Oxidative stress, Schizophrenia

### INTRODUCTION

Schizophrenia is clinical syndrome of variable but profoundly disruptive psychopathology that involves cognition, emotion, perception and other aspect of behaviour. The disorder usually begins before age 25, persists throughout life and affects persons of all social classes. Although schizophrenia is discussed as if it is a single disease it probably comprises a group of disorders with heterogeneous etiologies and it includes patients whose clinical presentations, treatment response and courses of illness vary.<sup>1</sup>

Prevalence studies of schizophrenia in India report prevalence rate between 1.5 per 1000 and 2.5 per 1000. Annual incidence is 0.35 to 0.38 per 1000 in urban population and 0.44 per 1000 in the rural population.<sup>2</sup>

Increased free radical mediated breakdown of phospholipids has been observed in schizophrenia. Oxidative neuronal injury in the brain has been known to be associated with abnormal neurodevelopment, neurodegeneration or neuronal membrane impairment. These mechanisms play a very important role in the pathogenesis of schizophrenia.<sup>3</sup> MDA is the most widely

used marker of lipid peroxidation and free radical activity.<sup>4,5</sup> In the view of above facts, it was planned to study malondialdehyde as an oxidative stress marker in Schizophrenia.

## METHODS

The present study was carried out in the Department of Biochemistry, Indira Gandhi Government Medical College, Nagpur, Maharashtra, India. The study protocol was approved by the Institutional Ethical Committee. An informed written consent was obtained from all the study subjects who were enrolled in the study.

50 patients of first episode schizophrenia and 50 patients of chronic schizophrenia visiting psychiatry OPD were included in the study. 50 numbers of age and sex matched healthy and apparently normal controls were also selected for study. The patients and controls were in the age group of 20-50 years of both sexes.

Participants were selected on basis of detailed history and clinical examination.

### Inclusion criteria

#### Criteria for first episode schizophrenic patients

- Newly diagnosed schizophrenic patients with DSM IV criteria.<sup>6</sup>
- Patients of either sex between 20-50 years of age.
- No history of taking antipsychotic medication at any period of time before study.

#### Criteria for chronic schizophrenic patients

- Chronic schizophrenic patients diagnosed with DSM IV criteria.<sup>6</sup>
- Patients of either sex between 20-50 years of age.
- Patients on atypical antipsychotic medication.

#### Criteria for controls

- Age and sex matched healthy and apparently normal subjects.

### Exclusion criteria

- Acute infectious and inflammatory diseases
- Diabetes
- Smoking
- Hypertension
- Alcoholic
- Liver diseases
- Pulmonary diseases
- Renal diseases
- Ischemic heart disease
- Neoplastic diseases

- Subjects on vitamins and antioxidant supplementation.

### Biochemical investigations

After written informed consent, Fasting blood samples were drawn from antecubital vein and collected in EDTA bulbs. Samples were centrifuged for 15 min at 4500 rpm. Plasma was analysed immediately for levels of malondialdehyde.

#### Assay for lipid peroxide (malondialdehyde) in plasma<sup>7,8</sup>

The principle of this method is based on the fact that lipid peroxides condense with 1-methyl-2-phenylindole (M.P.I.) under acidic conditions resulting in the formation of chromophore. To determine specifically lipid peroxides in serum or plasma they are precipitated along with serum or plasma proteins to remove water soluble MPI reactive substance.

The level of lipid peroxide is expressed in terms of MDA, which is unstable. Tetramethoxy propane, which is converted quantitatively to MDA in the reaction procedure, is used as standard. The chromophore formed during reaction has absorbance maximum at 586nm.

### Procedure

- A 7.6 mM solution of 1-methyl-2-phenylindole (M.P.I.) was prepared immediately prior to use in 33% methanol in acetonitrile.
- 650 µl aliquot of M.P.I. was placed in each test tube to which was added 200 µl of plasma.
- The test tubes were mixed and 150 µl of 10 M HCL was added. After mixing once more, the tubes were sealed and incubated for 60 minutes at 45o C.
- After incubation the tubes were chilled on ice bath and spun at 10,000 rpm for 5 minutes to remove debris.
- The absorbance at 586 nm was measured and subtracted from the blank value obtained by replacing plasma with water.
- A calibration graph was prepared using 2 µmol/L, 4 µmol/L, 6µmol/L, 8 µmol/L, of 1,1,3,3, tetra methoxypropane in 20 mm Tris HCL buffer, pH 7.4. (Figure – 1).

### Calculation

$$\text{Plasma malondialdehyde} = \frac{\text{Abs T}}{\text{Abs S}} \times \text{conc. of Std. } (\mu\text{mol/L})$$

The data collected was expressed as mean and standard deviation (S.D.) and statistically evaluated by Student's unpaired 't' test. P-value <0.05 was taken as significant, whereas P-value <0.01 was taken as highly significant. P-value >0.05 was considered statistically non-significant (NS).

**RESULTS**

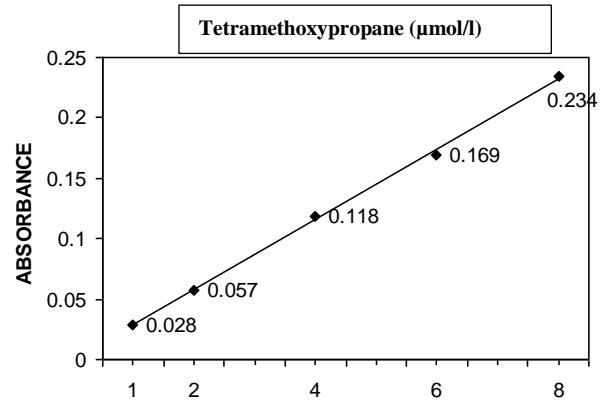
All the cases (First episode and chronic schizophrenics) and controls in the study were divided into 3 groups.

Group A: It consists of 50 first episode schizophrenic patients.

Group B: It consists of 50 chronic schizophrenic patients.

Group C: It consists of 50 age and sex matched apparently healthy normal subjects.

Present results in Table 2 show highly significant increase in the levels of plasma MDA in first episode schizophrenic patients (Group-A) ( $4.44 \pm 0.80 \mu\text{mol/liter}$ ) as compared to controls (Group-C) ( $3.34 \pm 0.71 \mu\text{mol/liter}$ ) ( $p < 0.01$ ).



**Figure 1: Standard graph for malondialdehyde.**

**Table 1: Age and sex distribution of cases and controls.**

	Group A (n=50)	Group B (n=50)	Group C (n=50)
Male	31	30	28
Female	19	20	22
M:F	1.63:1	1.5:1	1.27:1
Age in years (Mean ± SD)	$30.88 \pm 6.50$	$32.98 \pm 4.36$	$33.74 \pm 9.14$

Table 3 shows highly significant increase in the levels of plasma MDA in chronic schizophrenics (Group B) ( $4.23 \pm 0.65 \mu\text{mol/l}$ ) as compared to controls (Group C)

( $3.34 \pm 0.71 \mu\text{mol/l}$ ) ( $p < 0.01$ ). Table 4 shows no significant difference in plasma MDA levels in first episode schizophrenics (Group A) and chronic schizophrenics (Group B).

**Table 2: Levels of plasma malondialdehyde (MDA) in first episode schizophrenic patients (Group A) and controls (Group C).**

Parameter	Group-A(n=50) (mean ± SD)	Group-C(n=50) (mean ± SD)	P-value**
MDA(µmol/litre)	$4.44 \pm 0.80$	$3.34 \pm 0.71$	<0.01

\*\*P-value < 0.01 was taken as highly significant.

**Table 3: Levels of plasma malondialdehyde (MDA) in chronic schizophrenic patients (Group B) and controls (Group C).**

Parameter	Group B (n=50) (mean±SD)	Group C (n=50) (mean±SD)	P-value**
MDA(µmol/litre)	$4.23 \pm 0.65$	$3.34 \pm 0.71$	<0.01

\*\*P-value < 0.01 was taken as highly significant.

**Table 4: Levels of plasma malondialdehyde (MDA) in first episode schizophrenic patients (Group A) and chronic schizophrenic patients (Group B).**

Parameter	Group A (n=50) (mean ± SD)	Group B (n=50) (mean ± SD)	P-value
MDA(µmol/litre)	$4.44 \pm 0.80$	$4.23 \pm 0.65$	NS

#P-value > 0.05 was taken as statistically nonsignificant.

Table 4 shows no significant difference in the level of plasma malondialdehyde (MDA) in first episode schizophrenic patients (Group A) and chronic schizophrenic patients (Group B).

## DISCUSSION

Schizophrenia is a multifactorial disorder characterized by disturbances of thinking, social activity, language, perception, affect and volition.<sup>9</sup> Numerous studies have focused on roles of free radicals in the pathogenesis of neuropsychiatric disorders. It has been demonstrated that free radical-mediated neuronal dysfunction has roles in the pathophysiology of schizophrenia.<sup>10</sup> We studied plasma malondialdehyde (MDA) level, as a marker of oxidative stress in schizophrenic patients and controls.

Present results in Table 2 show highly significant increase in the levels of plasma MDA in first episode schizophrenic patients (Group-A) as compared to controls (Group-C) ( $p < 0.01$ ). Present findings correlate with findings of Arvindakshan M et al, Khan M, Mahadik SP et al, Surapaneni KM.<sup>11-14</sup>

Arvindakshan M et al<sup>11</sup> observed significantly higher levels of plasma thiobarbituric acid-reactive substances (TBARS) in never medicated (first episode) schizophrenic patients as compared to controls.<sup>11</sup> Surapaneni KM (2007)<sup>14</sup> reported significant increase in erythrocyte MDA levels in patients with schizophrenia, as compared to controls. Increase in MDA levels in first episode schizophrenics indicates ongoing oxidative injury at the very onset of psychosis.<sup>13</sup>

Present findings (Table 3) show highly significant increase in the levels of plasma MDA in chronic schizophrenics (Group-B) as compared to controls (Group-C) ( $p < 0.01$ ). Our findings correlate with the findings of Uma Devi P and Chinnaswamy P, LI Hui-chun, Dusica Pavlovic et al, Rukmini MS et al, Gora Dadheech, Arvindakshan M.<sup>11,15-18</sup> Rukmini MS et al found increased levels of malondialdehyde in schizophrenic patients as compared to normal controls.<sup>18</sup> Zhang XY, Tan YL et al found MDA levels were elevated in patients with a chronic form of schizophrenia as compared with normal controls.<sup>20</sup> Arvindakshan M also observed significantly increase in levels of MDA in chronic schizophrenics (medicated) as compared to controls.<sup>11</sup>

Present results maintained fair correlation with the findings of McCreadie RG et al, Ben Othmen L, Sarandol A, Kirli S et al, Zhang XY et al, Kuloglu M et al, Herken H et al et al.<sup>20-25</sup> Increased MDA in chronic schizophrenics indicates oxidative damage in chronic schizophrenia.<sup>24</sup> In present study Table 4 shows no significant difference in plasma MDA levels in first episode schizophrenics (Group-A) and chronic schizophrenics (Group-B). Our result is also in accordance with Arvindakshan M, who reported no

significant difference in the levels of plasma TBARS in the never medicated schizophrenics (first episode) and medicated schizophrenics (chronic schizophrenics).<sup>11</sup>

We observed plasma MDA levels were significantly increased in both first episode schizophrenics and chronic schizophrenics as compared to controls. Increased MDA levels in schizophrenic patients in our study may be due to increased oxidative stress. When we compared levels of MDA in first episode schizophrenic and chronic schizophrenics, we did not find significant difference.

## CONCLUSION

Above findings in present study suggest the possibility of increased oxidative stress and early involvement of the defective antioxidant system in schizophrenia.

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