



## SERUM MBL 2 WITH RISK GENOTYPING (RS1800450/CODON 54) IN SCHIZOPHRENIA PATIENTS: A HOSPITAL BASED STUDY IN SOUTHERN ODISHA

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### ABSTRACT

**Introduction:** Schizophrenia is a chronic psychiatric disorder characterized by delusions, hallucinations, cognitive deficits, and social dysfunction. Emerging evidence indicates that immune system dysregulation, particularly involving components of the innate immune system such as Mannose-Binding Lectin 2 (MBL2), may contribute to the pathogenesis of schizophrenia. Genetic variations, particularly at codon 54 of the MBL2 gene, may affect serum levels and influence disease susceptibility.

**Aims:** Estimation and Correlation of routine biochemical parameters and serum MBL2 level with MBL gene polymorphism (codon 54; rs1800450) in cases with schizophrenia and in healthy controls.

**Methodology:** A cross-sectional study was conducted taking 60 diagnosed patients of schizophrenia and age- and sex-matched 40 healthy controls. Serum MBL2 levels were assessed using ELISA kit, genotyping was done using RT-PCR and RFLP. Data were analysed using IBM SPSS 22.

**Results:** Serum MBL2: lower in schizophrenia patients ( $244.03 \pm 220.0$  ng/mL) compared to controls ( $330.17 \pm 243.2$  ng/mL,  $p = 0.003$ ). The analysis of MBL2 gene polymorphism showed AA, AB and BB genotypes 42 (70.0%), 13 (21.67%), and 5 (8.33%) in cases respectively whereas AA, AB and BB genotypes were found in 27 (62.50%), 12 (35.0%) and 1 (2.50%) in controls. Total cholesterol and triglycerides levels were significantly different among the above genotypes while HDL and LDL did not show any difference.

**Conclusion:** This study explores the link between MBL2 level with risk genotype (homozygous BB variety) which alter the innate immunity, may serve as a potential biomarker for screening and risk prediction for the schizophrenia spectrum disorders.

**Keywords:** Schizophrenia, MBL2, Risk Genotyping.

### INTRODUCTION

Schizophrenia is a chronic, heterogeneous psychiatric disorder characterized by disturbances in thought processes, perception, emotional responsiveness, and social interactions.

The clinical presentation includes positive symptoms (e.g., delusions, hallucinations), negative symptoms (e.g., anhedonia, social withdrawal), and cognitive impairments.<sup>1</sup>

The global burden of schizophrenia is significant, affects approximately 24 million people or 1 in 300 people (0.32%) worldwide. This rate is 1 in 222 people (0.45%) among adults.<sup>2</sup> It is not as common as many other mental disorders. The current and lifetime prevalence of schizophrenia spectrum disorder in India were 0.41% and 1.41% respectively.<sup>3</sup>

The prevalence of lifetime suicide attempts in those with schizophrenia ranges from 20% to 40%. It was estimated that one in every 20 individuals with schizophrenia will commit suicide.<sup>4</sup> The increased mortality among patients with schizophrenia has been attributed to unhealthy lifestyles common among this population (i.e., lack of exercise, unhealthy diet and excessive smoking and alcohol



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intake), treatment-related adverse events, the suboptimal treatment of concomitant physical illnesses, and suicide.<sup>5</sup>

### Schizophrenia is a Public Health Challenge:

People with schizophrenia often experience human rights violations both inside mental health institutions and in community settings. Stigma against people with this condition is intense and widespread, causing social exclusion, and impacting their relationships with others, including family and friends. This contributes to discrimination, which in turn can limit access to general health care, education, housing, and employment. During humanitarian and public health emergencies, extreme stress and fear, breakdown of social support, isolation and disruption of health care services and supply of medication can occur.

Schizophrenia is multifactorial, involving genetic, neurodevelopmental, and environmental contributors. Other risk factors associated with schizophrenia are infections, pregnancy and birth complications, dopamine dysregulations drugs and substances abuse. Notably, immune dysregulation and inflammation have emerged as important biological pathways associated with the disorder.<sup>6,7,8</sup> Mannose-binding lectin (MBL), a component of the innate immune system, plays a key role in the recognition and clearance of pathogens through the lectin pathway of complement activation. MBL is a large plasma glycoprotein belonging to the collectin (collagen and lectin) family of proteins.<sup>9</sup> Each MBL polypeptide contains four domains: a) A Cysteine rich N-terminal region involved in oligomerisation; b) A collagen like domain that makes up the long stalk of the molecule; c) A short alpha helical; hydrophobic neck region; d) C- terminal, carbohydrate – recognition domain.<sup>10</sup>

MBL is encoded by the MBL2 gene, located on chromosome 10q11.2–q21. MBL has a promoter region containing regulatory elements responsible for gene expression and four exons of the gene which are the coding regions. MBL2 comprises 7,461 bases translating into MBL protein of 248 amino- acids.<sup>11,12</sup>

The Lectin pathway of complement activation is initiated through MBL-MASP and Ficolin MASP cascades. MASP-1 activates MASP-2 which cleave complement factor and c4 and c2 combine to form c3 convertase.<sup>13</sup> MBL may also interact directly with cell surface receptors and thereby promote opsonophagocytosis by a complement-independent pathway<sup>14</sup>, mediate HIV binding and opsonization by modifying virus trafficking and viral antigen presentation. MBL releases cytokine and interleukin which regulate inflammation. MBL with peripheral blood mononuclear cell release tumor necrosis factor (TNF).<sup>15</sup>

However, MBL is not a typical acute phase protein, because its response is generally demonstrated by

the individual MBL levels and genetic variations.<sup>16,17,18</sup> Polymorphism in the MBL2 gene can significantly impact the levels and functional activity of MBL which in turn affects the individual's susceptibility to infection and autoimmune diseases. Promoter polymorphism affects MBL serum level H/L (550 H/L), X/Y (221X/Y), DEL (324 to 329), P/Q (+4 P/Q).<sup>19</sup> Exon 1 polymorphism at codon 54, 57 (allele B/D) and Exon 4 polymorphism at codon 223 (allele A/O) with various other combinations of polymorphism lead to MBL2 haplotypes which are associated with varying levels of MBL expression and functional activity. Single nucleotide polymorphisms (SNPs) in exon 1 and promoter region of MBL2 have been functionally characterized in regulating serum MBL (sMBL) levels. SNPs in exon 1 include rs5030737/codon 52; rs1800450/codon 54; and rs1800451/codon 57, jointly referred as MBL2 structural variations, out of which rs800450 and rs1800451 are involved in replacement of glycine with di-carboxylic acids.<sup>20</sup> Among these, SNP of rs1800450, located at codon 54 in exon 1, is of particular interest due to its impact on MBL oligomerisation and stability, leading to functional deficiency.<sup>21</sup>

### Importance of Mbl2 (Molecule and Gene Polymorphism) in Scizophrenia Patients:

Due to various public health challenges this is the first of a kind molecular and genetic study planned in Southern Odisha (INDIA) for early diagnosis and genetic predisposition knowledge of schizophrenia spectrum disorder which can aid in better management and prognosis. Genetic screening with lifestyle modification and appropriate therapy may be scope for preventing the social burden of schizophrenia.

#### Aims & Objectives:

- i. Estimation of routine biochemical parameters and serum MBL2 level in cases with schizophrenia and in healthy controls.
- ii. Comparison of MBL2 gene polymorphism (codon 54; rs1800450) in cases and healthy controls.
- iii. Correlation of MBL2 gene polymorphism with serum MBL2 level and other biochemical parameters in patients with schizophrenia.

### MATERIALS AND METHODS

This was a hospital-based case–control study conducted at the Department of Biochemistry in collaboration with the Department of Psychiatry, M.K.C.G. Medical College and Hospital, Berhampur, Odisha from November 2022 to March 2024. Study participants included 60 schizophrenia patients (cases) diagnosed per DSM-5<sup>22</sup> and ICD-10 criteria<sup>23</sup> and 40 age- and sex-matched healthy controls. Ethical approval was obtained from the

Institutional Ethical Committee, and informed written consent was taken from all the participants.

**Selection of Cases:**

**Inclusion Criteria:** Both sexes were included in our study aged 18 to 65 years. Newly diagnosed patients with schizophrenia (according to DSM5 / ICD 10 criteria) with no other systemic or neurological disorders affecting cognitive functions were taken.

**Exclusion Criteria:** Mental retardation, Neurodevelopmental disorder, Major depression, recurrent generalized anxiety, OCD, Alcohol dependence, Cocaine abuse other than schizophrenia patients and schizophrenia cases already on treatment were excluded from the study.

**Sample and Data Collection:** Demographic data and blood samples of the newly diagnosed cases were collected from OPD and bedside from the department of psychiatry and samples of controls were collected from healthy volunteers for laboratory investigations. Informed consent was taken from both cases and controls. 5ml of whole blood was collected from medial cubital vein in a dry, sterile disposal syringe under aseptic conditions. 3ml of blood was kept in serum

separator tube for half an hour at room temperature and then centrifuged at approximately 2000 to 3000 rpm for 10 to 20 minutes for biochemical parameters. 2 ml of whole blood was collected in EDTA vial for genetic study.

The serum sample was analyzed for FBS, LIPID profile, LFT, RFT and soluble MBL protein. On the day of collection, biochemical parameters were measured by TOSHIBA TBA120FR auto analyzer following internal and external quality control measures. Precautionary measures were taken to prevent hemolysis of samples. In an aliquot 1 ml of serum was stored in -20 °C for estimation of serum soluble MBL protein by ELISA kit (Bioassay Technology Laboratory). The EDTA vial containing whole blood was stored in 2-8 °C for genetic study (MBL2 gene polymorphism- codon 54; rs1800450).

**Estimation of Serum Mbl2:** Serum soluble MBL2 levels were measured using a commercial human ELISA kit (Bioassay Technology Laboratory, Cat. No E4304hu) following manufacturer protocols.<sup>24</sup> Optical density was read at 450 nm and MBL2 concentrations (ng/ml) were calculated using a standard curve.

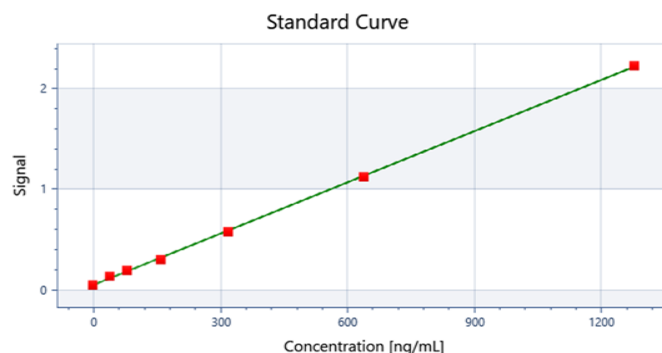


Figure 1: Standard Curve Showing Serum Soluble MBL2 Levels by Using Commercial Human ELISA Kit

**Genetic Analysis:**

Genomic DNA was extracted from EDTA blood using the phenol-chloroform method. DNA

quality was verified using NanoDrop spectrophotometry and 0.8% agarose gel electrophoresis.

#	Sample Name	Conc.	Units	Factor	A260	mm	260/280	260/230
	BLANK							
17	BLANK	30.468	ng/μL	50.00	0.6094	10	1.73	0.63
18	BLANK	113.244	ng/μL	50.00	2.2649	10	1.77	1.37
19	BLANK	294.254	ng/μL	50.00	5.8851	10	1.82	1.80
20	BLANK	302.585	ng/μL	50.00	6.0517	10	1.80	1.83

Figure 2: Dna Quality and Quantity Check by Spectrophotometer

Genotyping of MBL2 SNP rs1800450 was performed using a TaqMan RT-PCR assay (Thermo Fisher Scientific, Assay ID-C 2336609-20<sup>25</sup>) on the

QuantStudio 5 System. Genotypes were determined based on amplification curves for homozygous, heterozygous, and wild-type alleles.

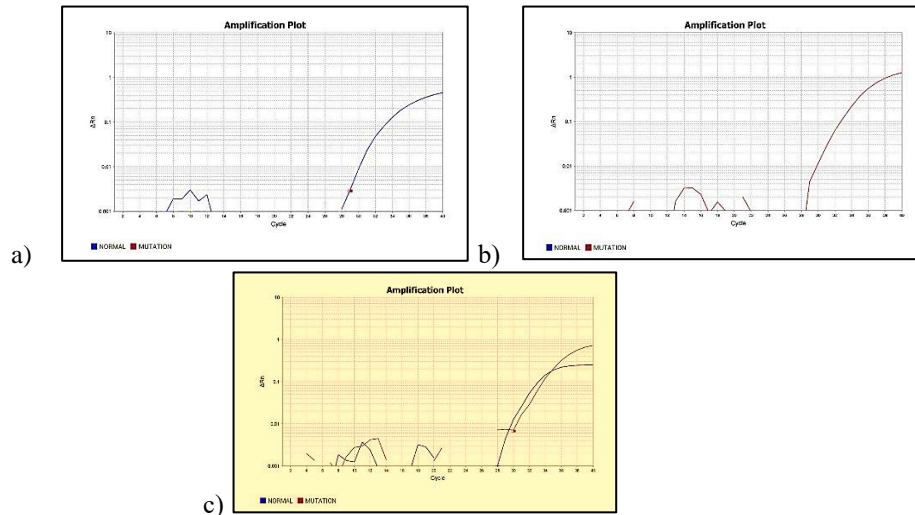


Figure 3: Real Time PCR Amplification Plot for A) Normal MBL2 Expression; B) Homozygous MBL2 expression; c) Heterozygous MBL2 expression

### Statistical Analysis:

Data were analysed using IBM SPSS version 22. Continuous variables were compared using one-way ANOVA, while categorical data were analysed with the Chi-square test. Hardy-Weinberg equilibrium was assessed for genotype distributions. A p-value of <0.05 was considered statistically significant.

This study investigated serum MBL2 protein levels and MBL2 gene polymorphisms in 60 schizophrenia patients and 40 healthy controls between November 2022 and March 2024. Demographic parameter, various routine biochemical parameters, special parameter serum MBL protein and genetic analysis results were recorded and analysed for both cases and controls.

### RESULTS

Table 1: Age and Biochemical Parameters of both Cases and Controls (N= 100)

Parameters	Cases with Schizophrenia (n=60)	Healthy Control (n=40)	Mann-Whitney Test (p value)
Age (in years)	30.58 ± 10.69	32.75 ± 12.29	0.941
Fasting plasma Sugar (mg/dl)	99.87 ± 39.0	89.8 ± 12.5	0.268
Total Cholesterol (mg/dl)	150.73 ± 34.24	135.53 ± 22.64	<b>0.010</b>
Triglycerides (mg/dl)	170.93 ± 105.94	110.65 ± 34.98	<b>0.010</b>
HDL- Cholesterol (mg/dl)	42.13 ± 14.40	40.70 ± 8.15	0.824
LDL- Cholesterol (mg/dl)	72.23 ± 25.67	72.65 ± 20.34	0.571
Total Bilirubin (mg/dl)	0.66 ± 0.39	0.54 ± 0.25	0.370
Direct Bilirubin (mg/dl)	0.15 ± 0.08	0.13 ± 0.05	0.366
SGOT (mg/dl)	40.51±20.90	26.70 ± 11.04	<b>0.001</b>
SGPT (mg/dl)	32.38 ± 22.43	22.58 ± 9.39	<b>0.034</b>
Urea (mg/dl)	24.65 ± 8.23	22.65 ± 7.61	0.158
Creatinine (mg/dl)	0.74 ± 0.17	0.67 ± 0.43	<b>0.011</b>

Table 2: Comparison of Serum MBL2 Level between Cases with Schizophrenia and Healthy Control (N= 100)

Special Parameter	Cases with Schizophrenia (n=60)	Healthy Control (n=40)	Mann-Whitney Test (p value)
Serum MBL2 (ng /mL)	244.03 ± 220.0	330.17 ± 243.2	<b>0.003</b>

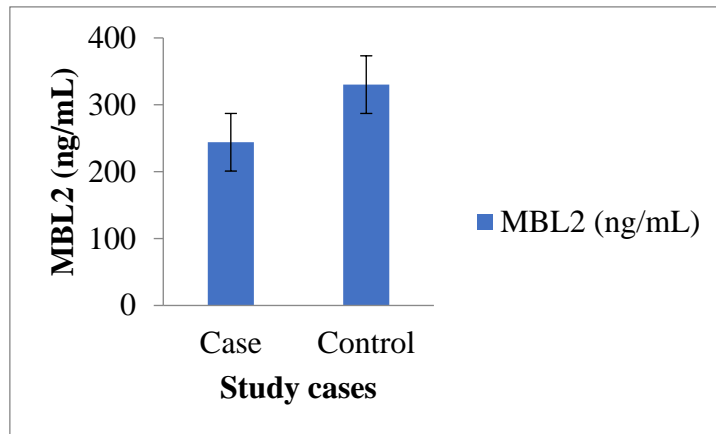


Figure 4: Comparison of Serum MBL2 Level between Cases with Schizophrenia and Healthy Controls.

Serum MBL2: Significantly lower in schizophrenia patients ( $244.03 \pm 220.0$  ng/mL) compared to controls ( $330.17 \pm 243.2$  ng/mL,  $P = 0.003$ ). Further, ROC curve was plotted for the comparison of serum

MBL2 level between cases with schizophrenia and healthy controls. The area under the curve was 0.68 with Sensitivity Rate: 0.88 and Specificity Rate: 0.42.

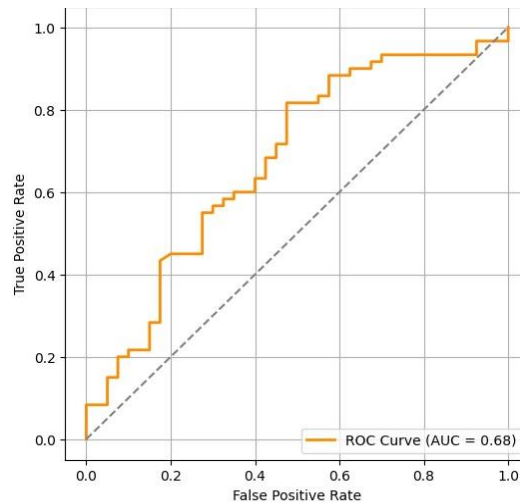


Figure 5: ROC Curve for the Comparative Analysis of Serum MBL2 Level between Cases with Schizophrenia and Healthy Controls.

#### MBL2 Gene Polymorphisms:

The analysis of MBL2 gene polymorphism by RT-PCR using Taqman assay between cases with schizophrenia and healthy controls showed AA, AB and BB genotypes in 42 (70.0%), 13 (21.67%), and 5 (8.33%) cases respectively whereas AA, AB and

BB genotypes were found in 27 (67.50%), 12 (30.0%) and 1 (2.50%) case respectively in controls. The distribution of MBL2 genotypes between cases and control groups did not show any statistically significant difference ( $p = 0.208$ ).

Table 3: Distribution of MBL2 genotypes between cases with schizophrenia and healthy controls (N= 100)

MBL2 genotypes	Cases with Schizophrenia (n=60)	Healthy Controls (n=40)	X2 Test; P Value
AA	42	70.00 %	3.143; 0.208
AB	13	21.67%	
BB	5	8.33%	

#### Distribution of MBL2 Genotypes between Cases with Schizophrenia and Healthy Controls:

The dominant and recessive models of MBL2 polymorphisms showed no significant association

between the cases and controls ( $p$  value = 0.229; 0.435 respectively).

Table 4: Distribution of MBL2 Genotypes (Dominant Model) Between Cases and Controls (N= 100)

MBL2 Genotype (Dominant Model)	Cases With Schizophrenia (N=60)		Healthy Controls (N=40)		X2 Test; P Value
	Count	Percentage	Count	Percentage	
AA/AB	55	91.67 %	39	97.50 %	1.448;
BB	5	8.33 %	1	2.50 %	0.229

Table 5: Distribution of MBL2 Genotypes (Recessive Model) between Cases and Controls (N= 100)

MBL2 Genotype (Recessive Model)	Cases With Schizophrenia (N=60)		Healthy Controls (N=40)		X2 Test; P Value
	Count	Percentage	Count	Percentage	
AA	42	70.00 %	25	62.50 %	0.611;
AB/BB	18	30.00 %	15	37.50 %	0.435

Among the three genotypes of MBL2 gene, serum MBL2 level was  $273.76 \pm 253.18$  ng/mL,  $186.72 \pm 69.17$  ng/mL and  $143.30 \pm 99.98$  ng/mL in cases

with AA, AB and BB genotypes. There were no significant differences ( $p = 0.278$ ) in the values of serum MBL2 level among the genotypes.

Table 6: Comparison of Serum MBL2 Level in Cases with Schizophrenia with Respect to MBL2 Genotypes (N=60)

Cases with Schizophrenia	MBL2 'AA' Genotype (N=42)	MBL2 'AB' Genotype (N=13)	MBL2 'BB' Genotype (N=5)	Kruskal Wallis Test (P Value)
Serum MBL2 (ng/mL)	$273.76 \pm 253.18$	$186.72 \pm 69.17$	$143.30 \pm 99.98$	0.278

Table 7: Categorisation of Serum MBL2 Level in Cases with Schizophrenia with Respect to MBL2 Genotypes (N= 60)

Cases with Schizophrenia	MBL2 genotypes	Very Low Serum MBL ( $\leq 100$ ng/ml)	Low Serum MBL (100-300 ng/mL)	Normal Serum MBL ( $> 300$ ng/ml)	P Value
		AA	3.33 %	56.44 %	
AB	1.66%	18.26%	1.66%		
BB	3.33%	4.98%	0%		

The allelic frequency of 'A' and 'B' allele in cases was 0.81 and 0.19 and in controls was 0.80 and 0.20 respectively. The table showing a higher frequency

of a allele in both cases and controls and a significant distribution of alleles in the case group was observed ( $p= 0.02$ ).

Table 8: Allelic Distribution of MBL2 Gene between the Cases with Schizophrenia and Healthy Control

MBL2 allele	Cases (n=60)	Healthy Controls (n=40)
'A' allele	0.81	0.80
'B' allele	0.19	0.20
Hardy-Weinberg equilibrium ( $\chi^2$ test; p value)	5.427; <b>0.02</b>	0.352; 0.553

## DISCUSSION

Schizophrenia (SZ) is a multifactorial psychiatric disorder with emerging evidence implicating immune dysfunction, including complement system dysregulation. The involvement of infection and immune activation in Schizophrenia raises the possibility that genetic variants that influence the susceptibility or immune response to certain infections may determine whether an individual has higher risk of developing the disease or not. This study explored the role of mannose-binding lectin 2 (MBL2) — a key component of the innate immune system—in schizophrenia through serum level analysis and genotypic evaluation.

In our study we have included 60 cases of schizophrenia and 40 age and sex matched healthy controls. The mean age of the cases and controls were  $30.58 \pm 10.69$  years and  $32.75 \pm 12.29$  years respectively ( $p=0.941$ ). In our study, the biochemical parameters like FBS, lipid profile (TC, TG, and HDLc), LFT (TBIL, DBIL, SGOT, SGPT), RFT (serum Urea and Creatinine) were estimated and compared in cases and controls (Table 1). The mean  $\pm$  SD of fasting blood sugar in cases ( $99.87 \pm 39.0$  mg/dl) were higher as compared to healthy controls ( $89.8 \pm 12.5$  mg/dl); yet not statistically significant ( $p = 0.268$ ). People with schizophrenia are at higher risk of developing type 2 Diabetes due to overall poor physical health, poor

health care, unhealthy lifestyles, high stress levels and side effects of antipsychotic drugs (Clozapine and Olanzapine).<sup>26,27</sup>

Abnormalities in glucose metabolism, including resistance to insulin actions; as a result of chronic low-grade inflammation in schizophrenia cases; might be a cause of higher circulating sugar level in drug naive patients. In our study we found that mean values of total cholesterol (mg/dl) ( $150.73 \pm 34.24$ ,  $135.53 \pm 22.64$ ;  $p=0.010$ ) and serum TG (mg/dl) ( $170.93 \pm 105.94$ ,  $110.65 \pm 34.98$ ;  $p=0.010$ ) in schizophrenia cases were significantly higher compared to that of healthy controls.<sup>26,28</sup>

Chronic inflammation in schizophrenia might be an etiological factor disrupting lipid metabolism and turnover, which in turn reflect as raised serum lipid parameters. Genes involved in lipid metabolism (e.g., FADS1/2, APOE, SREBF1) show altered expression or polymorphisms in schizophrenia.<sup>29</sup> However, patients with schizophrenia express abnormal membrane lipid composition, potentially due to disturbed redox regulation. Oxidative stress can also affect serum lipids and cause dyslipidaemia. Thus, an alteration in redox regulation can be a common factor linking abnormalities of both serum and membrane lipids in schizophrenia<sup>26,28</sup> and there were no significant differences in the value of the serum HDL cholesterol and LDL cholesterol. In LFT parameters, SGOT and SGPT level were significantly high in cases as compared to healthy control yet with in the normal biological reference range.

Distribution of MBL concentrations on the categories very low  $\leq 100$  ng/ml, low 100-300 ng/mL, normal  $> 300$  ng/ml is indicated.<sup>30</sup> With a 100 ng/ml cut-off, 8.33% of the patients in very low category, 80% of cases in low category were observed in our study.

In our study, serum MBL2 level was significantly lower in schizophrenia cases ( $244.03 \pm 220.0$  ng/mL) as compared to healthy controls ( $330.17 \pm 243.2$  ng/mL). MBL deficiency indicates aetiological heterogeneity among patients of schizophrenia. Activation of the peripheral innate immune cytokine pathways whether because of an immune challenge or stress leads to increased proinflammatory cytokine production and decreased neurotrophic support and neurogenesis in brain areas important to behaviour and cognition.<sup>30,31</sup> The aberrant MBL-Lectin pathway leads to weaken immune system, subthreshold immune reaction and in turn predisposing the subject to more prone for infection and decrease host defence. There were no epidemiological studies with serum MBL2 level in schizophrenic cases in India. Apart from schizophrenia serum MBL2 level have been identified in various studies such as recurrent aphthous stomatitis, dengue, Diabetic Nephropathy, Malaria.<sup>32,33,34,35</sup>

Serum MBL2 levels and its genetic polymorphisms are distributed widely in the general population. In our study, the true positive rate is 88% indicating a higher screening value of serum MBL protein in detecting new cases of schizophrenia yet with a low specificity rate (42%) as multiple factors like infections, diabetes and other chronic inflammatory conditions might alter the serum level. (Figure-5)

Out of multiple polymorphisms observed in the structural gene components of MBL haplotype, we have observed and studied the Exon 1; codon 54 at rs1800450 (C/T, Transition substitution). Out of 100 participants (60 schizophrenia cases and 40 controls) 67% have normal homozygous genotype (AA), 27% have AB genotype, 6% have mutated homozygous genotype (BB). The homozygous BB variant was more prevalent (8.33%) in schizophrenia cases in comparison to in controls (2.50%) with a p value of 0.208 (Table 3), indicating the mutant varieties are more prone to develop the disease than the wild varieties. So, we have analysed further taking dominant and recessive models, which showed that homozygous B variety was more associated with the disease trait compared to homozygous A or heterozygous AB variety (Table 4&5).

The concentration of serum MBL level in patients of schizophrenia was higher in AA genotypes with a decreasing trend among AB and BB genotypes pointing towards an increased risk of MBL deficiency in our study. Exon 1 of the MBL gene encodes the signal peptide, a cysteine rich domain and multiple copies of a repeated Glycine motif (Gly-X-Y), typical for the triple helix formation of collagen structures. Ficolin proteins share certain structural similarities with MBL protein, and they also have a collagen-like sequence, which enables the assembly of homo-trimeric structures. Single point mutation in codon 54 of MBL gene causes a replacement of glycine (GGC) with aspartic acid to (GAC) (Gly54Asp) producing unstable MBL variant proteins which are easily degraded to lower oligomeric forms and probably have a shorter half-life in the circulation (Gared 2009<sup>21</sup>; Larsen et al., 2004<sup>36</sup>). This might lead to decrease biological function so also reduced serum concentration. (Table 6&7)

Besides, SNPs at codon 54 of Exon 1, other SNPs at regulatory and coding region of MBL gene contributes towards the altered expression of the above protein. Apart from genetic influences, serum MBL protein is affected by multiple heterogeneous factors affecting its serum concentration.

Furthermore, allelic distribution study revealed that the case group, deviated from Hardy-Weinberg equilibrium, suggesting a possible role of genetic divergence in disease association. We found that 'A' allele is the dominant allelic frequency observed in both cases and controls (0.81; 0.80) compared to B allele (0.19; 0.20). The 'B' allele frequency is quite common among Asian and Caucasian population

(0.11- 0.17)<sup>37</sup> which is very similar to our study finding indicating a genetic drifting of affected individuals which needs further investigation.

#### Implications:

The findings reinforce the involvement of immune mechanisms in schizophrenia and suggest that MBL2—through both its serum level and genetic variants—may contribute to disease vulnerability or progression. Although limited by sample size, low serum MBL2 and B allele frequency distribution in our study, supports a potential immunological deficit linked to disease pathophysiology. However, larger population based genetic studies are required to confirm these associations of serum MBL2 and its genetic variance as potential biomarkers.

#### CONCLUSION

This study is the first to report in India; a significant reduction in serum MBL2 levels in patients with schizophrenia, suggesting a potential role of MBL2 in the pathophysiology of the disorder. The findings propose that serum MBL2 may serve as a diagnostic biomarker, with potential utility in population screening and prognostic assessment. The MBL2 (Exon 1- codon54/rs1800450) polymorphism was observed at a higher frequency compared to other Asian population in both schizophrenia patients and controls, with a trend toward decreased serum MBL2 levels in the recessive genotype (BB) model was noted, which was statistically significant. This highlights the need to investigate other genetic contributors in conjunction with MBL2 to clarify its role in disease susceptibility.

Further research involving larger cohorts and comprehensive genetic analyses is warranted to substantiate these findings and fully elucidate the clinical relevance of MBL2 as a biomarker in schizophrenia.

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