

## **HIGHLIGHTS**

The domain of Psychiatry has undergone profound changes in recent times. The addition of Psychiatric Genetics - a comparatively new enterprise to the medical fraternity has opened many a new avenue for our apprehension of the complex basis of behavioral disorders. Most of the behavioural disorders are complex in nature i.e. they do not follow Mendelian inheritance as it happens in cases of single gene disorder. Over the last two decades most of the genetical research in psychiatry was done exclusively on Schizophrenia, as it is one of the most tragic psychotic disorders which affects 1% of the general population and partially on bipolar disorders. However in the present investigation, a relatively rare but not uncommon psychotic disorder i.e. delusional disorder was considered because of the the following unique features:

1. Delusional disorder (a thought disorder) is a monosymptomatic psychotic disorder i.e. it has only one symptom, where as other psychotic disorders represent a cluster of signs and symptoms. Hence it can be considered as a model psychotic disorder.
2. Delusional disorder is clinically a heterogeneous illness. Delusional symptom is referred to as paranoid condition, associated with more than 100 different conditions like other psychiatric diseases, medical conditions, pharmacological agents etc. So the question may be raised as to how delusion is formed in delusional disorder and in spectrum of aforementioned conditions. Do they share similar etiopathologic mechanism(s)?
3. No systematic study was pursued on delusional disorder. Even epidemiologic informations are meagre and etiopathology of delusional disorder is not properly understood. Psychological, anatomical and biochemical studies have failed to reveal any predisposing role in its causation. Genetic investigations are too scanty to be reviewed. But limited family studies do support the familial clustering of the trait and thereby increasing the likelihood of genetical underpinnings. Immunological investigations on a related paranoid disorder suggest that paranoid disorder may be linked to autoimmune mechanisms.

4. The most stimulating aspect for undertaking the present venture was that the patients with different psychiatric conditions do not influence the social fabric. However, patients with delusional disorder change the societal structure resulting in high marital breakdown, low fecundity etc. and thereby adding extra burden to the family members as well as on society. Moreover, patients with delusional disorder often implicate their spouse and family members and resorting to judicial intervention rather than reporting their mental health condition to the clinicians.

These unique features stimulated to perform an exploratory immunogenetic as well as cytological study to understand the underlying etiopathologic mechanism(s) of delusional disorder. To our knowledge, this study is the first reported attempt to comprehend the relationships between delusional trait and HLA genes. As noted above, delusion is associated with different conditions; the present investigation was beautifully designed which comprised two groups: one group represented chiefly delusional disorder while other group included paranoid schizophrenia (thought disorder), mood congruent delusion (depression with psychotic features) and early Alzheimer's disease with psychotic features (an organic brain disorder). Unlike delusional disorder, all these disorders of second group had delusion as one of the symptoms. The formation of delusion in monosymtomatic delusional disorder as well as in other three disorders from second group whether bears the similar etiological mechanisms or not.

Some interesting and new observations were made from this investigation. These are:

1. Some of the alleles of HLA-A locus are strongly associated with delusional and other disorders with delusion.
2. Though delusion is seen in a wide spectrum of conditions, the mechanism(s) of delusional formation may not be the same in all these conditions i.e. they may not be linked genetically. However, delusional disorder and paranoid schizophrenia may have similar etiological underpinnings.
3. Based on the findings, a new hypothesis on the etiopathological mechanism(s) of paranoid conditions by implicating HLA system is proposed.