CHAPTER 6

Summary & Conclusion

5. SUMMARY & CONCLUSION

Delusional disorder, the contemporary conceptualization of paranoia, is an uncommon condition characterized by the presence of one or more nonbizarre delusions and the relative absence of associated psychopathology. Delusion has attracted enormous attention because it occurs in a large number of psychiatric as well as medical conditions. No systematic research on paranoia took place for more than half a century and modern investigations on delusional disorder were not done earlier. Hereditary factors and association with inherited personality factors may play a part, in the psychological maldevelopment. However, there is an urgent need for the study of extended case series utilizing modern neurophysiological and neuropsychological investigative methods.

In the present investigation, a set of two different disorders namely delusional disorder and schizophrenia were considered, as paranoid (delusional) disorders are thought to overlap with schizophrenic disorders. Both the disorders have delusion as one of the symptoms. Amongst these disorders only delusional disorder is monosymptomatic i.e., it represents delusion as the only symptom, while schizophrenia posses multiple symptoms of which delusion is one of them. The interesting aspect of this investigation was to study the etiological basis of delusion in delusional disorder as well as in schizophrenia.

The objectives of the present investigation were two folds. In one way, it was speculated that like schizophrenia- a closely related thought disorder, it may involve dysregulation of dopaminergic neurotransmission and for this purpose genetics of dopamine receptors (DR), its main synthesizing enzyme tyrosine hydroxylase (TH) and dopamine transporter (DAT) were considered. In the other way, Plasma homovanillic acid (pHVA) was investigated to have a more detailed view of brain dopamine function in delusional disorder as it acts as an indicator of central dopamine turnover.

The roles of immune dysfunction and inflammation in schizophrenia have long been described by the scientists. It was speculated that like schizophrenia- a closely

related thought disorder, delusional disorder may also involve immune dysfunction and inflammation and for this purpose C-reactive protein (CRP) was estimated in the patients.

Polymorphism of dopamine receptor genes, tyrosine hydroxylase and dopamine transporter genes have been studied in the present investigation in 100 delusional disorder patients and equal number of age and gender matched healthy controls, 30 unrelated patients with schizophrenia and equal number of healthy donors. The healthy donors in both the cases were matched for all the sociodemographic variables.

Estimation of plasma homovanillic acid was done by HPLC method with electrochemical detection for all the patients with delusional disorder. An equal number of age and gender matched healthy donors having similar sociodemographic variables have been considered for the study.

Brief Psychiatric Rating Scale was employed for all the 100 delusional disorder patients to measure the psychopathology profile of the patients with delusional disorder as a whole and also in its different clinical subgroups.

Latex agglutination slide test was performed for the measurement of C-reactive protein in the patients with delusional disorder as well as in the controls. For this purpose a total number of 47 unrelated patients and an equal number of age and gender matched healthy donors belonging to the same sociodemographic condition have been considered.

Association of DR, TH and DAT-

The association studies of dopamine receptor genes, TH and DAT genes yielded interesting results in all patient groups with delusional disorder. D2S allele was found to be strongly associated with the disease along with the TH1 allele with a moderately strong association. It may be conceived that the polymorphism of the DR and/or TH gene could be the part of the genetic basis underlying the hyperdopaminergic state and delusional etiology of the disease. However, the formation of delusion in schizophrenia may have a different etiology.

High level of pHVA-

High level of pHVA was found in the delusional disorder patients when compared with the healthy controls suggesting the dopamine hypothesis of the disease. Earlier studies on major psychoses including schizophrenia-a closely related thought disorder have documented that the higher pHVA psychosis is a dopamine psychosis which may have a familial origin. Consistent with this result we observed the familial clustering of the disease.

Study of CRP-

The present study found that the elevated serum levels of CRP were associated with the medication status of the patients with delusional disorder. The drug naïve patients showed higher value. Our result is in consistence with the previous scientific evidences that suggest an increase in the stress hormone like norepinephrine which is regulated by a catecholamine specifically dopamine, may activate the inflammatory arm of the immune system and triggers the expression of genes that cause chronic, low-grade inflammation. This inflammation is characterized by the degree of the levels of CRP.

Suggestive Conclusions:

i) A strong association of dopamine D2S allele has been confirmed in this study using PCR-SSP. Dopamine D2S allele may be used as a biological marker of delusional disorder. As the pattern of dopamine receptor alleles are determined in the offsprings contributed both by the mother and father which persists through out the life time, it can be assumed that D2S allele of dopamine D2 receptor gene may act as the trait marker for the disorder.

ii) The incidence of D2S was not significant in the patients with schizophrenia rather D1 allele was found to be significantly associated with this disorder suggesting that the etiology of the formation of delusion may be different in the delusional disorder and the schizophrenia.

iii) Highly significant positive correlation was found between the pHVA in the patient with the delusional disorder compared to the controls. Further, our results showed that there is an association of high pHVA was with high BPRS score led us to the conclusion that the pHVA could be used as a state marker for the disease.

iv) The sociodemographic data of our study represents that delusion of infidelity or jealous type is the most common type among the Indian Bengali population followed by persecutory type. The prevalence or clustering of delusional disorder as well as paranoid features in the first degree relatives of the patients with delusional disorder is quite high and thus strengthen the involvement of genetic factors in this disorder.

v) Elevated serum levels of CRP in drug naïve patients with delusional disorder paved the way to the direction of its association with the medication status of the patients. It further strengthens our dopamine hypothesis of the disease as dopamine triggers the expression of genes indirectly that cause chronic, low-grade inflammation, characterized by the degree of the levels of CRP.