

Original Article

Gene-environment interactions in schizophrenia: features from a Pakistani family

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Abstract

Schizophrenia is a chronic psychosis with a worldwide prevalence of 1%. It is diagnosed on the basis of psychiatric symptoms and till now no biochemical test is available for its diagnosis. It is considered one of the most costly disease in terms of diagnosis and treatment. Its heritability content is considered to be up to 80% but still it is unknown whether it's a pure genetic disease. It is considered a polygenic multifactorial condition where both genes and environment have roles in disease development. In the present study we selected a family with multiple schizophrenic patients and have identified some reasons for disease development. It is estimated from study that in Pakistan there is gender bias in schizophrenia unlike the worldwide data because more of males are affected in the selected family. For the males the age at onset was higher compared to females and the affected individuals were unmarried and unemployed. Parental consanguinity was another important determinant studied and was identified that three of four offsprings of cousin marriage were schizophrenic. It was concluded from the present study that along with inherited nature of schizophrenia importance of shared environment cannot be ruled out. There is an urgent need to educate general population about the consequences of disorder so that people take it cautiously and it may be treated early and its bad consequences be reduced.

Key words: Family based study, Genetics, Schizophrenia

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INTRODUCTION

Schizophrenia is a chronic psychosis with 1% prevalence worldwide (Rössler *et al.*, 2005). This condition is known from 1896 when it was first described as Dementia praecox by Kraepelin (1896). The term schizophrenia was coined in 1911 by Bleuler (1911) (Astrachan *et al.*, 1972). More than 100 years of research have not yet found the actual cause of this condition and both environmental and several genetic factors are considered to play part in the development of this disease. It is considered a polygenic and multifactorial condition (Mino and Oshima, 2006, Richards *et al.*, 2016) that is included in the top ten costly psychiatric illnesses.

Schizophrenia is a type of mental illness for which there is no prognostic marker available (Nielsen *et al.*, 2015). Even no biochemical test is till now considered gold standard for disease prognosis. It can mainly diagnosed on basis of

psychiatric symptoms. Both positive and negative symptoms are important in disease diagnosis. International criteria for diseases (ICD-10) and Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) criteria for psychiatric illnesses analysis are commonly implied as diagnostic strategy. In Pakistan ICD-10 is mostly used.

Case control analysis approach is usually implied to find the actual genetic content for disease association (Hirschhorn *et al.*, 2002) but in contrast family based approach not only gives the genetic content but also provide the insights of involvement for environmental factors (Thomas, 2010). Several genes involved in neurodevelopment are found associated with schizophrenia but no consistent results for a single gene are observed till now. So chances of involvement of shared environment are quite high. Heritability content of schizophrenia although high (up to 80%) but still studies reflect the effect of environment in disease

development. Based on the previous data available a family based analysis for schizophrenia is done to find the multifactorial nature of disease.

SAMPLE IDENTIFICATION AND ANALYSIS

A family having multiple patients suffering from schizophrenia was identified from Punjab, Pakistan. All the family members available were analyzed by trained psychiatrists from a public sector hospital for mental health Lahore following ICD-10 criteria for psychiatric disease identification. On the basis of this identification normal and schizophrenic patients were described. Demographic data was

collected by interviewing the normal family members. Information about age, marital status, education and employment status was evaluated. Age at onset of disease was evaluated by first appearance of symptoms. Information about sharing of environment was also collected.

All statistical analysis was performed using social science statistics software (<http://www.socscistatistics.com>).

RESULTS

A total of five affected individuals were initially identified of which one was expired before our analysis and a total of four affected individuals were studied in the family (Fig. 1).

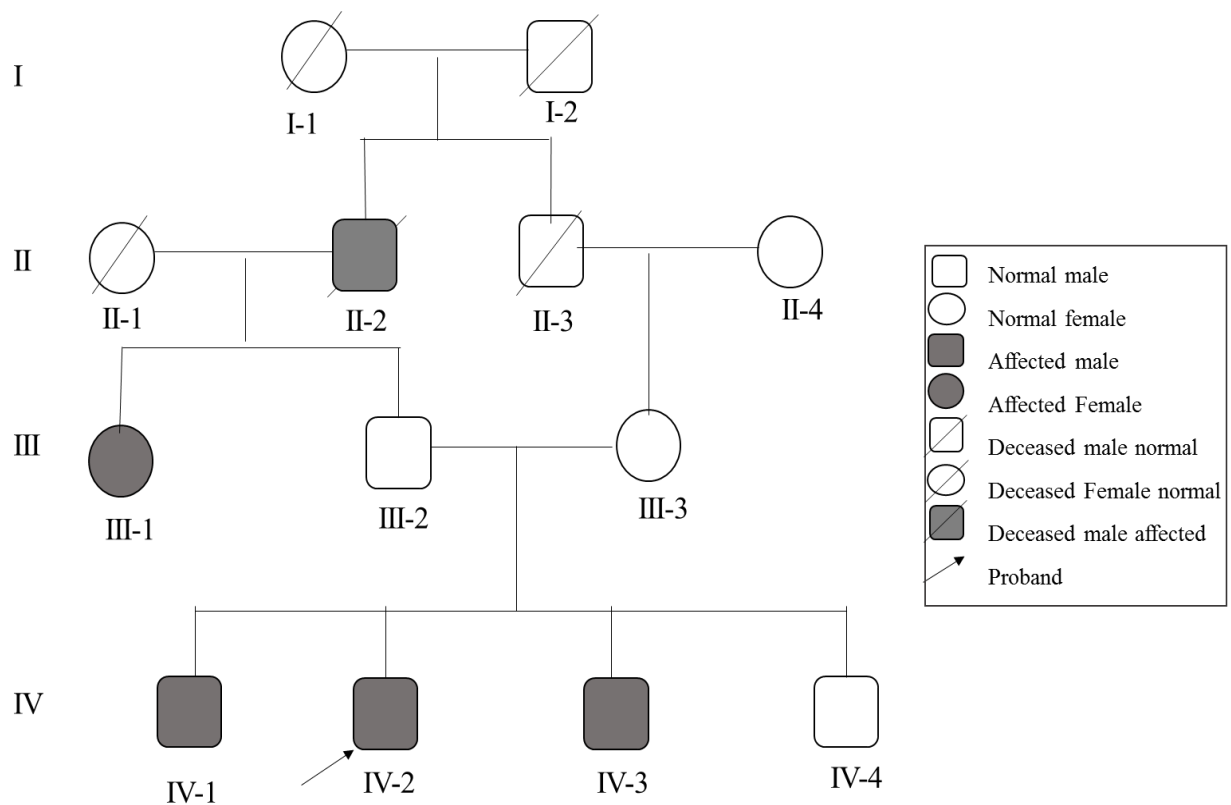


Figure 1: Pedigree of Family SEF-1 identified with multiple members affected with schizophrenia

Of these four schizophrenic patients three were siblings and were male. While their paternal aunt was also affected. Parents of three affected sibs III-2 and III-3 were psychologically normal. While the father of III-1 who was expired before analysis was said to be one of the sufferers of same condition. There is no reliability as family says "he was having same

symptoms like his daughter". Age was observed at the time of analysis and was noted that IV-1, IV-2 and IV-3 were of ages 40 years, 38 years and 28 years respectively. While the age of III-1 was 65 years at time of observation. The schizophrenics in the family were diagnosed first at ages of 31 years, 32 years, 25 years and 27 years (IV-1, IV-2, IV-3, III-1) (Table I).

All of them were unemployed and unmarried although affected males had got 10 years of education at least. III-1 was uneducated, unemployed and unmarried. IV-1,

IV-2 and IV-3 were the product of first cousin marriage. While III-1 was product of non cousin marriage although her parents belonged to the same caste group.

Table I: Basic information about family selected

		Total	Male	Female
Number	Total	8	5	3
	Affected	4	3	1
Mean age* (Years)	At onset	28.75± 3.3	29.3± 3.7	27
	At observation	42.7±15.7	35.3±6.4	65
Marital status*	Single	4	3	1
	Married	0	0	0
Parental cousin marriages*	Yes	3	3	0
	No	1	0	1

*only schizophrenic patients

DISCUSSION

Family based analysis for disease diagnosis are always considered better tools for identification of multifactorial conditions. The main reason is that these help not only in identification of shared genes but also the shared environment. In the present study we are reporting a family with multiple affected members. One of the four affected members was a female. Although international literature complies on the fact that both males and females have a same ratios to be affected with schizophrenia. In our selected family it was not the case for which there were many reasons. One of which might be the fact that randomly this family had more of affected males. Other reason is due to the social pressures and family burdens, normal members of families are usually reluctant to provide information about females in the family specially the disease status in females. That is why the information about the females was not provided by family.

Age at onset of disease ranged from 25 years to 32 years (average 28.75± 3.3 years). There was no difference in age at onset for males and female although males were presented with an average increased 29.3± 3.7 years of age compared to only affected female. This finding is in contrast to international literature that states that males are normally presented with early age at onset (Eranti et al., 2013). Interesting feature was that in contrast to

two affected elder brothers IV-3 had a quite early age at onset (25 years). This finding relates to the impact of environment where sharing of environment increased chances of early disease onset.

All the patients were unemployed rendering the effect of unemployment on disease onset. The 24 years old normal sibling (IV-4) was employed. Many studies reveal the effect of certain stress conditions in relation to psychosis (Marwaha and Johnson, 2004) including effect of unemployment and disturbed marital status. This study signifies that there is a genetic predisposition for schizophrenia in individuals that leads to increased risk of schizophrenia when the appropriate environment is provided. As Tsuang (2000) described that genetic predisposition along with environmental insults leads to neurological and brain damage and ultimately to schizophrenia. It is concluded from the study that shared environmental factor cannot be overruled as one of the cause of schizophrenia as it reduces the age at onset. There is also an urgent need to educate general population about the disease and its impacts so that patients may be diagnosed early and treated.

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