

THE PREVALENCE OF SCHIZOPHRENIA IN RELATIVES OF SCHIZOPHRENIC PATIENTS

L C C Lim, L P Sim

ABSTRACT

This study examines the prevalence of schizophrenia in 871 first-degree relatives of schizophrenic probands (N=121) and 658 first-degree relatives of age-matched controls. The controls (N=126) were medical inpatients referred for psychiatric opinion in a general hospital. Diagnoses in the probands fulfilled the ICD criteria for schizophrenic psychoses. Information on the relatives were obtained from enquiry of the family history and the hospital case records. The prevalence of schizophrenia in first-degree relatives of schizophrenic probands was 22 times that of the medical controls (6.8% versus 0.3%) ($p < 0.05$). The result supports the observation that schizophrenia is a familial disorder.

Keywords: *Familial Study, Genetics, Psychiatric Morbidity*

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INTRODUCTION

Kraepelin⁽¹⁾ emphasized the importance of familial factors in his earliest descriptions of dementia praecox. Since then, many family studies have consistently reported increased risks of schizophrenia for first-degree relatives of schizophrenics compared to the general population⁽²⁻⁵⁾. Based on these results, schizophrenia has been widely considered to be a familial disorder. Pope et al⁽⁶⁾ reported that none of the total of 199 first-degree relatives of schizophrenics had an illness that satisfied DSM-III⁽⁷⁾ criteria for schizophrenia. Abrams and Taylor⁽⁸⁾ applied their own criteria to a sample of 128 first-degree relatives of schizophrenics and reported only two cases of schizophrenia, giving a lifetime prevalence of 1.6%. These two American studies were criticized for its small sample size, its lack of control sample and its lack of independent estimate of the frequency of schizophrenia in the general population⁽⁹⁾.

Most family risk studies were published in the West and there is a dearth of information in the East. The authors decided to carry out a preliminary survey to determine the prevalence of schizophrenia in the parents and siblings of schizophrenic patients in Singapore. We present our findings in this paper.

METHODS

A consecutive series of 121 patients (60 male, 61 female) admitted to a government psychiatric hospital for the treatment of schizophrenia were included in the study. The 126

non-schizophrenic (50 male, 76 female) age-matched controls were drawn from medical inpatients referred for psychiatric opinion in a general hospital.

Ideally, the diagnosis should be based on a personal interview with the individual being examined, an interview with a relative who knows the individual, and an examination of all available psychiatric medical records. From a practical standpoint, personally interviewing all index patients (probands) and their relatives can be difficult. As a result of limited resources, we were unable to carry out interview studies in the probands and the diagnoses were derived from hospital case records. In the controls, all patients were interviewed by one of the authors (LCCL) and a family history of psychiatric illness was enquired into in every case. In order to minimise errors in the diagnoses of the probands, the recorded symptoms were checked against the criteria listed for Schizophrenic Psychoses in the International Classification of Diseases (ICD) classification system⁽¹⁰⁾. They must, in clear consciousness, exhibit at least two of the following features: (a) disorder of thought judged to be of schizophrenic kind; (b) persistent or recurrent hallucinatory experiences; (c) persistent delusions with a persecutory, grandiose or somatic content; (d) the presence of shallow, capricious or incongruous mood; (e) ideas of thought control or other feelings of influence and passivity; (f) catatonic motor disorders.

A questionnaire designed to collect demographic data was used and a family history of schizophrenia was systematically recorded. A family tree was constructed and this was supplemented by information available from the patients' case records. However we did not attempt to differentiate between the subtypes of schizophrenia. The limitation of our methodology will be pointed out in the discussion.

RESULTS

There were a total of 871 first-degree relatives (242 parents, 629 siblings) of schizophrenic patients and 658 first-degree relatives (246 parents, 412 siblings) among the controls. The offsprings of these patients were excluded from the study because most of them were under the age of eighteen. Table I shows the demographic characteristics of our sample. The racial distribution reflects the distribution in the general population. The mean age was 36.4 years (s.d.=11.1) for the schizophrenic probands and 33.8 years (s.d.=9.8) for the controls. The mean age of onset of schizophrenia for the probands was 27.0 years (s.d.=8.8). Majority of the schizophrenic patients were single, unemployed, and readmissions to the hospital.

The prevalence of schizophrenia in the first-degree relatives of schizophrenic patients was 6.8%. This was in distinct contrast to 0.3% in the relatives of non-schizophrenic controls.

Department of Psychological Medicine
National University Hospital
5 Lower Kent Ridge Road
Singapore 0511

L C C Lim, MBBS, MRCPsych, FAMS
Senior Lecturer

Woodbridge Hospital
Jalan Woodbridge
Singapore 1954

L P Sim, MBBS, MRCPsych, FAMS
Senior Registrar

Correspondence to: Dr L C C Lim
Genetics Section
Institute of Psychiatry
Denmark Hill
London SE5 8AF
England

Table I - Demographic Characteristics of Sample

		Schizophrenic Probands	
		No	(%)
Race	Chinese	103	(85.1)
	Malay	13	(10.8)
	Indian	5	(4.1)
Age (years)	Mean (s.d.)	36.4	(11.1)
Age of Onset (years)	Mean (s.d.)	27.0	(8.8)
Marital Status	Single	84	(69.4)
	Married	33	(27.2)
	Widowed/Separated	4	(3.4)
Occupation	Unemployed	77	(63.7)
	Housewife/Student	18	(14.9)
	Employed	26	(21.4)
Class Status	First Admission	19	(15.7)
	Readmissions	102	(84.3)

The prevalence of schizophrenia in the parents and in the siblings were 6.6% and 6.8% respectively. There was no affected parents in the controls and the prevalence for schizophrenia was only 0.5% for the siblings of controls (Table II.)

Table II - History of Schizophrenia in first-degree relatives

Schizophrenic Illness	Relatives of Probands		Relatives of Controls		p Values
	No	(%)	No	(%)	
All Relatives					
- Yes	59	(6.8)	2	(0.3)	< 0.05
- No	812		656		
- Total	871		658		
Parents Only					
- Yes	16	(6.6)	0	(0.0)	<0.05
- No	226		246		
- Total	242		246		
Siblings Only					
- Yes	43	(6.8)	2	(0.5)	<0.05
- No	586		410		
- Total	629		412		

DISCUSSION

The most important finding in this study is that there is increased morbidity of schizophrenia in the first-degree relatives of schizophrenic patients. The prevalence of schizophrenia in first-degree relatives of 6.8% was comparable to other published studies in the West (Table III). Our result is lifetime prevalence that have not been age adjusted and so are underestimates of morbid risk.

Family study is one of the most widely used tools in psychiatric genetics. We use the data from such studies to answer the question, does a psychiatric illness run in families? If genes are etiologically important to a disorder, then relatives of ill individuals (probands) should be at greater risk of the illness than relatives of normal controls. The demonstration that schizophrenia is a familial disorder has important implications for the cause of this condition. The prevalence of schizophrenia in first-degree relatives of schizophrenic probands -

Table III - Prevalence of Schizophrenia in first-degree relatives

Study	Criteria	First Degree Cases	Relative Sample	Prevalence %
Stephens et al (1975)	ICD-8	12	332	3.6
Tsuang et al (1980)	Feighner-like	20	375	5.3
Guze et al (1983)	Feighner-like	4	111	3.6 *
		9	111	8.1 **
Baron et al (1985)	DSM-III	19	366	5.8
Present Study	ICD-9	59	871	6.8

* Definite schizophrenia

** Definite and Probable schizophrenia

in our study, was twenty-two times that of the controls. Our data support earlier reports that schizophrenia is a familial disorder⁽²⁻⁵⁾ and they are consistent with previous evidence that genetic factors play a major etiologic role in schizophrenia^(11,12).

Although a genetic hypothesis predicts that a disorder will be familial, it is important to point out that a disorder may be familial for other reasons. Family members share a common culture and a common environment, hence familial environmental factors may confound genetic relationships. The finding of familial transmission cannot be unambiguously interpreted. However the failure to find familial transmission can be taken as a strong sign that a disorder does not have a substantial genetic component.

The authors are acutely aware of the limitation of recording family history from the patients and the hospital case records. Our result probably include some cases of "non-affective psychosis". The category of "non-affective psychosis" denotes a plethora of related conditions such as: paranoid disorder, schizoaffective disorder and atypical psychosis. The ideal family study uses double-blind, case-controlled methodology in which diagnoses of relatives are made independent of any knowledge of the proband's diagnostic status. The variations in results between the different studies can be explained by the differences in methodology. The prevalence is higher in studies where "definite" and "probable" schizophrenia were considered as a group. Guze et al⁽⁴⁾ studied 111 first-degree relatives of schizophrenic probands, the prevalence of schizophrenia fell from 8.1% to 3.6% when only "definite" schizophrenia was considered. In general, in studies where operationally defined schizophrenia was utilized, the morbid risk was much reduced^(13,14). To improve on the quality of our data, some important methodological features such as the use of stringent operational criteria, the blind and independent diagnosis of patients and relatives, and the use of structured interview schedules would have to be employed in future prospective study.

Most schizophrenic patients remained single, thus the first-degree relatives recorded were mainly siblings and parents. In our study, a total of 40 offsprings were recorded and the majority of these were less than 18 years old. This group was excluded from the analysis because they did not reach the age of risk of developing schizophrenia. The small number of offsprings reflects the small number of married schizophrenic probands (N=33). The fertility of schizophrenic individuals is reported to be 30% to 70% below that seen in the normal population⁽¹⁵⁾. There was only a single case of schizophrenia

among the offsprings. The index patient was a 52-year-old married lady who has been suffering from schizophrenia for the past thirty-five years. There was no history of schizophrenia in her parents or her siblings. However her 22-year-old daughter, the youngest of her six children, was afflicted by the same condition.

Other than determining the familial nature of schizophrenia, family studies can also clarify the familial relationship between schizophrenia and other psychiatric disorders. To date, there is no consistent relationship between schizophrenia and the other major psychiatric syndromes, including affective disorder, schizoaffective disorder, paranoid disorder, anxiety disorder, and alcoholism⁽¹⁶⁻²¹⁾. There is thus a continual need for family studies to be conducted in order to clarify these relationships.

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ANSWER TO ELECTROCARDIOGRAPHIC CASE

Diagnosis: acute infero-postero-lateral myocardial infarction

DISCUSSION

The ECG shows Q waves in leads I, II, aVL and V6; coved and elevated ST segments in II, III, aVF, V5-6; tall broad R waves in V1-3; ST depression with tall upright T waves in V1-2. A few minutes after this ECG was completed, he was noted to have sustained ventricular tachycardia on the ECG monitor with clenching of teeth and twitching of limbs. He was subsequently cardioverted with DC shock 200 joules.

The interesting feature in this ECG is the tall R wave in V1 with an R/S ratio of > 1 . The differential diagnosis of a tall R wave in V1 includes: (1) Posterior myocardial infarction, (2) Right ventricular hypertrophy, (3) Right bundle branch block, (4) Left-sided accessory pathways of the Wolff-Parkinson-White syndrome, (5) Duchenne muscular dystrophy, (6) Mirror image dextrocardia, (7) Dextroposition of the heart, (8) Normal variant.

The posterior wall of the heart is the posterobasal or dorsal aspect of the left ventricle and is that part of the left free wall situated between the lateral (superior) and the inferior walls, towards the base of the left ventricular cone. As none of the leads in the conventional 12 lead ECG look directly at the posterior surface of the heart, diagnosis of true posterior infarction must be made from *inverse* or *mirror image* changes in leads facing the uninjured anterior surface of the heart, viz in leads V1-3⁽¹⁾. The changes of acute posterior wall infarction are: (i) tall and slightly widened R waves in V1-3, with R:S ratios > 1 and R wave duration of 0.04 seconds or more,^(2,3) (ii) tall, upright and symmetrical T waves in leads V1-3, and (iii) depressed, concave-upwards ST segments in leads V1-2.

In the normal heart, the larger mass of the left ventricle compared to the right ventricle results in an initial small r wave (due to septal depolarisation from left to right) followed by a deep S wave in V1 (due to the dominant effect of the left ventricle). In acute posterior wall infarction, the loss of late posterior wall vectors allows the anterior wall vectors to

dominate and this is manifested in tall and broad R waves in V1-3. The T wave vector is always directed *away* from the ischaemic surface. Therefore in posterior infarction, the T wave is directed anteriorly, resulting in tall symmetrical T waves in V1-3. The T waves in the left lateral leads V4-6 are low and frequently inverted. Eisenstein et al showed that when the amplitude of the T wave in V2 minus the amplitude in V6 is 0.38mV or more, it had a sensitivity of 81% and a specificity of 75%⁽⁴⁾. The ST segment vector is directed *toward* the injured surface, in this case posteriorly where it would be *coved and elevated*. This is reflected in reciprocal changes in the anterior leads V1-3 which show *depressed, concave upward* ST segments.

Posterior myocardial infarction rarely occurs in isolation. It is nearly always associated with inferior⁽⁵⁾ and/or lateral infarction as shown in this example.

Nestico⁽⁶⁾ showed that the combination of a wide Q wave in aVF with an upright T wave in V1 is the best predictor of posterior wall myocardial infarction, with a sensitivity of 78%, a specificity of 89% and a predictive accuracy of 86%.

Arkin⁽⁷⁾ showed that the combination of an R wave duration greater than or equal to 0.04 seconds and an upright T wave in V1 had a specificity of 98%, a predictive accuracy of 80%, but a sensitivity of only 12%.

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