An Overview of the Genetic Influence of Schizophrenic Patients Treated at the Lakipadada Hospital

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Abstract Schizophrenia is a complex severe mental disorder with pathogenesis that involves many risk factors. Many studies have tried to examined the role of genes which responsible for the etiology of schizophrenia. The Lakipadada Hospital in Tana Toraja (Indonesia) has treated 2.322 outpatient and 81 inpatient of schizophrenic patients on the 2018. In January until April 2019, it has 500 outpatient and 18 inpatient. This study aims to describe the genetic influence of schizophrenic patients who are treated outpatient and inpatient at The Lakipadada Hospital from January to April 2019. The subjects consist of 101 persons, they are schizophrenic patients who traced to a family history of schizophrenia in the first, second and third generations, they are examined using Tools Brief Psychiatric Rating Scale (BPRS). The study was approved by the Ethics Commitee of Lakipadada Hospital. The datas will analyzed by using Pearson test for each items of BPRS then we use a multivariate analysis with linear regression to determine a constant item derived to the across generation. The Pearson's test determine 3 items from BPRS that have a strong relationship in every across generation, they are conceptual disorganization (r=0,474; p=0,00), suspiciousness (r=0,471; p=0,000) and hallucinatory behavior (r=0289; p=0,04). After a linear regression test, hallucinatory behavior item is constantly inherited in schizophrenic patients in every across generation (Anova: p=0,005, r=1,030 and r=0,995), ith Adjusted R Square 0,986. Hallucinatory behavior item of the BPRS are constantly inherited to each schizophrenic patient who has a genetic history of schizophrenia across generations.

Keywords Schizophrenia, Genetic influence, BPRS

1. Introduction

Schizophrenia is a complex severe mental disorder with pathogenesis that involves many risk factors. The prevalence of schizophrenia in the world about 1% of the population with an incidence rate of 1 per 10,000 people per year [1]. In the 2007, the prevalence of schizophrenia in Indonesia was 2 per mile, but in the 2013 increased to 2.6 per mile [2,3,5]. Symptoms in men usually occur at the end of childhood or early 20s, whereas in women in their 20s or early 30s [1].

Psychopathology in schizophrenia can be classified into three dimensions, they are consist of positive symptoms, negative symptoms and disorganization symptoms. The positive symptoms include hallucinations, delusion, excitement, odd behavior and hostility. The negative symptoms include blunt or flat affect, withdrawal, reduced motivation, poor emotional contact (quiet, difficult to talk), passivity and apathy. The symptoms of disorganization include speech, behavioral disorganization and disruption in concentration and information processing [2,3].

The etiology of schizophrenia is still unclear, but it is thought to involve genetic factors, perinatal and gestational factors, psychosocial stressors and neurochemical factors (dopamine hypothesis and serotonin hypothesis) [1,3,4].

Genetic factors play an important role of etiology schizophrenia. It has a significantly inheritance, complex and polygenic. In the twin studies, monozygotic twins have a 4-6 times risk than dizygotic twins. The risks of schizophrenia during life are as follows: in monozygotic twins (40-50%), dizygotic twins (10%), schizophrenic siblings (10%), children of one schizophrenic parent (10-15%) and children of both schizophrenic parents (30-40%). Linkage analysis based on the fact from the affected individuals concluded that they are received chromosomal material from the ancestor, it was explained why in the families had multiple affected individuals [8,9,23,24,26].

Several large meta-analyses have found strong evidence of numerous genetic linkages of 6p24-22, 1q21-25, 22q11-12, 5q21-33, 10p15-11, and 1q42 [6-9].

The Torajan ethnic has the high cases of schizophrenia among other ethnic in South Sulawesi. The Lakipadada Hospital in Tana Toraja (indonesia) has 2.322 schizophrenic outpatient and 81 inpatient on the 2018. At January until

April 2019, it has 500 schizophrenic outpatient and 18 inpatient.

The studies about genetic schizophrenia in Indonesia is still limited when compared with studies in other developed countries. Based on the background, this study aimed to describe the genetic influence of schizophrenic patients who are treated inpatients and outpatients at Lakipadada Hospital from January to April 2019.

2. Methods

2.1. Subjects

One hundred and one schizophrenic patients were recruited from Lakipadada Hospital. The subjects have family history of schizophrenia in the first, second and third generations, they are examined using Tools Brief Psychiatric Rating Scale (BPRS). The study was approved by the Lakipadada Ethics Commitee. Inclusion criteria included: (1). ICD-10 diagnostic criteria for schizophrenia; (2). Schizophrenic patients who have a family history of schizophrenia. Exclusion critera included is schizophrenic patients who have history of drug abuse.

2.2. Design and Procedure

This study was an observational analytic studies. The study was approved by the Lakipadada Ethics Commitee, in Lakipadada Hospital, Tana Toraja, Indonesia, and all experiments were performed in accordance with relevant guidelines and regulations. After a detailed explanation of the study protocols, all subjects and their family were given written informed consent for participating in this study and the publication of the results.

Each patient and family who came for treatment at the Lakipadada hospital was measured by Brief Psychiatric Rating Scale (BPRS) scale, then we analyzed each items on the Brief Psychiatric Rating Scale (BPRS) scale which tended to be derived from the previous generation.

Brief Psychiatric Rating Scale (BPRS) is a widely used instrument for asessing the positive, negative, and affective symptoms of individuals who have psychotic disorders, especially schizophrenia. It should be administrated by clinician who is knowledge able concerning psychotic disorder and able to interpret the constructs used in the assessment. Also considered is the individual's behavior over the previous 2-3 days and it can be reported by the patient's family [10].

2.3. Measurement

2.3.1. Psychometric Measures

The BPRS consists of 18 symptoms include somatic concern, anxiety, emotional withdrawal, conceptual disorganitation, guilt feelings, tension, mannerism and posturing, grandiosity, depressive mood, hostility, suspiciousness, hallucinatory behavior, motor retardation, uncooperativesness, unusual throught content, blunted affect, excitement and disorientation. It takes 20-30minutes for the interview and scoring. The rater should enter a number ranging from 1 (not present) to 7 (extremely severe). 0 is entered if the items is not assessed. First published in 1962 as a 16-construct tool by Drs.John Overall and Donald Gorham, the developers added two additional items, resulting in the 18-item scale used widely today to assess the effectiveness of treatment [10].

2.3.2. Statistical Analysis

The data was analyzed using statistical program (SPSS) and presented with tables. The data will be analyzed using Pearson's test then continue with a linear regression test to get the constantly inherited in schizophrenic patients in every across generation.

3. Result

3.1. Subjects Characteristic

The demographic characteristics of the subjects are shown in table 1.

Table 1. Demographicts of subject

Characteristics Subjects		Frequency	Persentage (%)
Gender	Male	51	50.5
	Female	50	49.5
Age (years)	15-20	1	0.99
	20-25	8	7.92
Mean	26-30	4	3.96
(42.32)	31-35	10	9.9
Median (40)	36-40	15	14.85
	41-45	6	5.94
	46-50	12	11.88
	51-55	7	6.93
	56-60	11	10.89
	61-65	3	2.97
	66-70	8	7.92
	71-75	3	2.97
	76-80	8	7.92
	81-85	2	1.98
	86-90	3	2.97
Education	Elementary school	23	22.77
	Junior high school	30	29.70
	Senior high school	19	18.81
	Diploma 3	3	2.97
	Bachelor	3	2.97
	Did no have education	23	22.77

Source: Primary data, 2019

The demographicts subject tables showed that the sample was mostly male (50.5%) with an average age of 42.32 years and the most sample education was junior high school level.

Based on the characteristics of the sample data, it obtained the most sex is male (50.5%), this is in accordance with the literature which states that schizophrenia is more commonly found in male than female [1,2,7,9].

The highest age in the sample was 36-40 years (14.85%), according to the literature, men had schizophrenia onset earlier than women, the peak age of onset for men was 15 to 25 years, for women of peak age it was 25 to 35 years, onset schizophrenia before the age of 10 years or after the age of 50 is very rare. Approximately 90 percent of patients are treated with schizophrenia between the ages of 15 and 55 years [1,8,9,10]. The most sample education is junior high school (40.7%), this is in accordance with the literature which states that in industrialized countries, schizophrenic patients are in low socioeconomic groups or groups who fail to exit the low socioeconomic group (downward drift hypothesis). The economic conditions become one of the reason why the patient education in our studies only at the level of junior high school. Another reason to support the education level is presence of cognitive dysfunction because of schizophrenia, so it causes limited academic ability [1,3].

3.2. The Genetic Influence of Schizophrenic Patients

Based on statistical results using Person test, there are 5 items of BPRS that are statistically significant and inherited genetically in schizophrenic patients. The statistical results of the Person test are shown in table 2.

Table 2. The Correlation Value of 18 items BPRS by using Pearson Test

Items of BPRS	The correlation value (p)		
	Significant at 0.05 level	Significant at the 0.01 level	No significant
Conceptual disorganization		0.000	
Suspiciousness		0.000	
Halucinatory Behavior		0.004	
Anxiety	0.012		
Unusual Thought Content	0.037		
Somatic concern			0.484
Emotional withdrawal			0.713
Guilt feeling			0/484
Tension			0.254
Mannerisme and posturing			0.754
Grandiosity			0.874
Depressive mood			0.373
Hostility			0.245
Motor retardation			0.899
Uncooperativeness			0.113
Blunted Affect			0.817
Excitement			0.945
Disorientation			0.89

Based on the results of the Pearson test, it determine 3 items from BPRS that have a strong relationship in every across generation, they are conceptual disorganization (r=0,474; p=0,00), suspiciousness (r=0,471; p=0,000) and hallucinatory behavior (r=0289; p=0,04). While the clinical symptoms likes somatic concern, emotional withdrawal, guilt feeling, tension, mannerism and posture, grandiosity, depressive mood, hostility, motor retardation, uncooperativeness, blunted affect, excitement and disorientation which are not statistically significant for schizophrenic patients. After the Pearson Test was carried out, it was continued by multivariate analysis using linear regression to find out the BPRS items that were inherited constantly and continuously across generations. The statistical results of Linear Regression are shown in table 3.

Table 3. The Correlation Value of significant BPRS by using Linear Regression

Items of BPRS (constant)	Coefficients (sig.)	ANOVA (sig.)	Adjusted R Square
Suspiciousness	0.046 and 0.667	0.084	0.979
Halucinatory Behavior	0.03 and 0.05	0.005	0.986

Based on the results of the analysis using linear regression it was found that the clinical symptoms of BPRS that were constantly inherited across generations were halucinatory behaviors (p_{ANOVA}: 0.005) with adjusted R Square value of 0.986 or 98.6%. It shows that the halucinatory behavior is a clinical symptom that is inherited constantly across generations by 98.6%, while 1.4% is still influenced by other variables not examined.

4. Discussion

Schizophrenia commonly has a chronic course albeit with fluctuating patterns, and cognitive disability. Its hallmark is psychosis, mainly characterized by positive symptoms such as hallucinations and delusions that are frequently accompanied by negative (deficit) symptoms such as reduced emotions, speech, and interest, and by disorganization symptoms such as disrupted syntax and behavior. Severe mood symptoms, up to and including manic and major depressive episodes, are present in many cases [11,12,15,17,18].

There are no diagnostic laboratory test for schizophrenia; instead, the diagnosis relies on clinical observation and self-report. Epidemiological studies over the last century using clinical phenotype, it has consistently shown the importance of genetic factors in schizophrenia. Psychiatric genetics has historically focused in large part on the study of schizophrenia and its epidemiology. It is well-established that the heritability of schizophrenia is > 80%, among the highest known for complex genetic disorders. 22q11.2 deletion syndrome (22q11.2DS; previously George syndrome and velocardiofacial syndrome) is the only

established genetic subtype of schizophrenia of proven clinical relevance. The association of 22q11.2DS with schizophrenia followed soon after the discovery in the early 1990s that the 22q11.2 deletion was the underlying molecular anomaly unifying several, seemingly distinct, clinical syndromes first described in the 1960s and 1970s [7,13,14,15,22,25,26].

Many of the studies determine that the genetic etiology of schizophrenia, include spontaneous mutations, reduced penetrance, and variable expressivity, are found in 22q11.2DS. Several studies have confirmed that 22q11.2DS accounts for approximately 1% of all cases of schizophrenia. Conversely, an estimated 22.5% of adults with 22q11.2DS develop schizophrenia or a related psychotic disorder [16,17,18,26].

22q11.2DS is also associated with the psychotic symptoms in schizophrenic patients such as auditory hallucinations and delusional. It is also explain the impact of 22q11.2DS on the inheritance of the next generation. Based on this study, we found that the clinical symptoms of BPRS that were constantly inherited across generations are halucinatory behaviors [19-26].

This study had several limitation. The limitation including: (1). Sample is still in small group, (2). Limitations of tools for detecting chromosomes that are responsible for inheritance of schizophrenia.

Future directions in this area include the following:

- Collection of sufficiently large samples and better methods of pedigree ascertainment to obtain power to detect linkage and then loci to chromosomal regions
- Application of large-scale family-based association tests across the whole genome.
- Resolution of genetic heterogeneity requires further work on phenotypic classification to identify clinical characteristics that can delineate genetically distinct groups.

5. Conclusions

These study was support that schizophrenia is associated with strongly genetic predisposition. It shows that the hallucinatory behavior is a clinical symptom that is inherited constantly across generations.

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