Outcome Study of Early Onset Schizophrenia

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Schizophrenia is a serious mental illness that often affects young people with an enormous impact not only on the patient and family, but society as a whole. The outcome of early onset schizophrenia is often poor with one quarter to one third having bad prognosis. Aims: The aims of this study were to observe the sociodemographic profile, the clinical presentation and to study the outcome of subjects presenting with first episode schizophrenia before the age of 18 years old. Method: This is a cross-sectional study of 100 consecutive patients diagnosed with early onset schizophrenia and who were followed up for at least two years or more in University Malaya Medical Centre. Results: About half of the subjects had an unfavorable outcome, who had significantly younger (<15 years old) age of onset of illness, longer duration of symptoms prior to their first contact, and impaired functioning. Conclusion: Strategies need to be implemented for early detection and intervention of schizophrenia especially those of early onset, so that subsequent disabilities can be prevented.

Key words: Early onset schizophrenia, outcome

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Introduction

Schizophrenia is a chronic recurring psychotic illness that characteristically affects quite young people and lasts a lifetime (1). Bleuler (2) estimated that between 0.5% and 1% of schizophrenic cases had their onset before age 10, and 4% before 15 years old. Prior to the 1960s the term "Childhood Psychosis" was applied to a heterogeneous group that included a variety of pervasive developmental disorder without hallucinations and delusions. In the early 1970s with the publication of the 3rd edition of Diagnostic and Statistical Manual of Mental Disorders (DSM – III), schizophrenia with a childhood onset was formally separated from autistic disorder. The question of how to view the disorder in children had raised several controversial issues. Early Onset Schizophrenia (EOS) is no longer included as a separate diagnostic entity; rather children with schizophrenia are diagnosed in the same way as adults (3), as some believe that early onset schizophrenia show no qualitative difference from adult onset schizophrenia (4).

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The diagnosis of schizophrenia can often be missed in early stages especially, among the young. Schizophrenia is essentially clinically quiescent until after puberty, the earliest symptoms are diagnostically subtle, non-specific and less prominent than the consequent disabilities and those disabilities are created during the early phase (5). Though early diagnosis and intervention is warranted (6), for a large number of schizophrenics, such treatment is often delayed (7) and quite commonly in the developing world, treatment is never even accessed (8). Though the outcome of schizophrenia is often said to be worse in developed countries, compared to developing countries (2), the associated cost and burden are extensive no matter which country the patient is from, and it still remains a fact that approximately 25% of the patients have a poor outcome (9,10, 11). Worse still, the outcome of early onset schizophrenia is often reported to be even poorer (12).

There is still limited local data on the pattern of EOS in Malaysia. It would be beneficial, if one understands the extent of the problem related to the outcome of EOS in a local setting, so more effective means can be implemented in the management of such cases. The aims of the study are to find out the clinical characteristics and risk factors associated with poor

outcome in EOS, so that appropriate steps could be planned to minimize the disabilities.

Methods

A sample of 100 consecutive patients who fulfilled the inclusion criteria were selected via the psychiatric out-patient clinic and in-patient psychiatric ward. Patient selected for the study were those who had a documented primary diagnosis of schizophrenia for at least two years, and had their first contact to University Malaya Medical Centre at the age of 18 years old or below to ensure a valid diagnosis of EOS. The nature of the research was explained to them and informed consent was obtained before formal assessment. Those with an onset of illness at 15 years old and below were grouped under "very early onset", while those with onset between 16 and 18 were grouped as "early onset".

The patients were interviewed to obtain: (i) Sociodermagraphic data such as age, sex, ethnicity, occupation, marital status and socioeconomic class. (ii) Clinical characteristics included detail history of presenting symptoms, duration of initial symptoms prior to their first contact, family history of mental illness and identifiable stressors. (iii) Functional status was assesed using the Global Assessment of Functioning (GAF).

The socioeconomic status that was obtained was based on the occupation of the parents at the time of interview. The social class was divided into I, II, III, IV and V. Social class one referred to professionals like accountants, doctors and lawyers. Social Class II comprised of intermediate group with managers, school teacher and nurses. Social Class III consisted of skilled non-manual workers like clerks, secretaries and shop assistants. Skilled manual and semi skilled manual workers like bus drivers, carpenters, agricultural workers and post-man etc. belonged to social Class IV and social Class V consisted of unskilled manual workers like labourers and cleaners (13).

The presenting symptoms were divided into positive symptoms, negative symptoms and both. The positive symptoms included third person auditory hallucinations, commenting voices, audible thought, thought insertion, thought withdrawal, thought broadcasting, somatic passivity and delusional perception. The negative symptoms included reduced volition, social withdrawal, reduced amount of speech and poor personal hygiene. The duration of initial presenting symptoms were classified into either less than 6 months or more than 6 months before their first contact with University Malaya Medical Centre.

Patients were then classified into either 'good', 'moderate', 'poor' or 'very poor' outcome categories. In the good outcome category, patients must be employed or schooling full time, had resumed their former roles in society (family, friends, married or living with some one), and were not seen to be mentally ill by family members or friends. Their GAF must be > 70 at the time of interview. Patients in moderate outcome category should be working or studying more than 50% of the time, and have friends but visit them infrequently. They must still posses definite schizophrenic symptoms but may be symptom free from time to time with medication. Their GAF must be 51-70 at the time of interview. Poor outcome category would consist of patients who worked less than 50% of the time and had symptoms 70% of time despite being on regular medication. They live in supervised homes and posses a GAF score of 40-50. Finally, the very poor outcome category would comprise patients who were unable to work or study, were symptomatic all the time and needed constant care and medication with a GAF of less than 40(15). However, for statistical convenience the former two were grouped under "favourable group" with a GAF of > 50 and the latter two were grouped under "unfavourable group" with a GAF of <50.

Results

Of the 100 subjects, there were 57 males and 43 females. The study population consisted of mainly Chinese (n=64), followed by Malays (n=19) and Indians (n=17). A majority of the subjects were single (n=97) with only 3 married. At the time of interview the mean age of the subjects was 22. 86 years (S.D = 4.69). Most of them (41%) were in the 21-25 years age group. About a third (34%) of them were between the age group 15 to 20 years and the remaining 25% were above 25 years old at the time of interview. The age at first contact with University Malaya Medical Centre ranged from 12 years to 18 years (mean 15.87 years, S.D.=0.7). Forty one percentage of them were 15 years and below ("very early onset") while 59% of them were between 16 and 18 years old ("early onset") when they were first

diagnosed to have schizophrenia. Most of the subjects belonged to lower socioeconomic groups i.e. Social Class V = 48%, IV = 26%, III = 21%, II = 5% and none from social class I. About two thirds (n=60) of the subjects were unemployed while the rest (n=40) were involved in some forms of employment or studying. Among those who were working, 33% (n=13) of them were students, 27% (n=11) were general workers, 22% (n=9) were shop assistants, 10% (n=4) were clerks and 8% (n=3) were teachers.

As for the duration of symptoms, 44% experienced symptoms for longer than 6 months before establishing first contact with psychiatric services, where else the remaining 56% waited for less than 6 months before seeking psychiatric help. Identifiable initial stressors were noted among the subjects (n=59). The most common stressor reported by these age group subjects during their first onset of illness were school related problems and examination pressure. This accounted for 66% (n = 40) of the stressors. The next common stressor was relationship problem 18% (n =10). The rest reported other stressors like family problem, work stress and sexual abuse. About half (n = 49) of the study population had positive family history of mental illness. Among these subjects, 36% (n=18) had first degree relatives with mental illness while the rest 64% (n =31) had second degree relatives with mental illness.

After assigning the patients into the "favourable" and "unfavourable" groups using the criteria delineated earlier, it was found that 49 patients fell into the "favourable" group and 51 patients fell into "unfavourable" group. The distribution of these 2 subgroups among the genders, ethnicity, age groups, marital status, social class and employment status is as stated in Table 1. Statistical analysis was then performed to ascertain if any risk factors could be identified. There was no difference in terms of outcome between the different genders, ethnic groups and social classes. However, it was observed that the age of onset of illness was significantly related to the outcome where the younger age group had the worse

Table 1: Sociodemographic data of favourable vs. unfavourable groups (n = 100)

	Favourable (n = 49)	(%)	Unfavourable (n = 51)	(%)	p value
Sex					
Male	30	61 %	27	53%	ns
Female	19	39 %	24	47%	
Age of Onset					
< 15 years	11	22 %	30	59%	
16 –18 years	38	78 %	21	41%	.004
Marital Status					
Single	46	94 %	51	100%	ns
Married/Divorced	3	6 %	0	-	
Race					
Malay	10	20 %	9	18%	
Chinese	29	60 %	35	68%	ns
Indian	10	20 %	7	14%	
Social Class					
II	3	6 %	2	4%	
III	11	22 %	10	20%	ns
IV	14	29 %	12	23%	
V	21	43 %	27	53%	
Occupational status					
Working/Studying	35	71 %	5	10%	.0006
Unemployed	14	29 %	46	90%	

out-come (p=0.0004). Similarly, employment of the subjects were significantly related to the outcome of the illness, where those who were unemployed or not studying were more likelybelong to the "unfavourable group" (p = 0.0006). Distributions of clinical characteristics between the "favourable" and "unfavourable" groups are shown in Table 2, and statistical analysis was performed to ascertain any significant differences. Duration of symptoms prior to the first contact with the health care system was significantly related to the outcome (p=0.004). The shorter the duration of initial presenting symptoms, the better was the outcome of the illness. However, there was no significant difference between the outcome and the type of symptoms, neither was there any significant difference between outcome and a positive family history of mental illness. Similarly, the presence of an identifiable stressor at the onset of illness did not have a bearing in whether a patient would belong to the "favourable" or "unfavourable" group.

Discussion

A century ago, schizophrenia, then known as *dementia praecox* was considered a chronic progressive illness leading to severe impairment in cognitive and social functioning. Poor outcome was considered to be almost inevitable. The development of antipsychotic drugs in 1950s released patients from long term hospitalization and increased the hopes of improving the outcome of this illness. However, this encouraging development also revealed a contrasting and somber reality that approximately 25% of the patients have a poor outcome (10, 11). This study revealed that half of the subjects (51%) had unfavourable outcome despite being in contact with psychiatric services. The era of treating psychotic disorders began in 1952 with the discovery of chlorpromazine, which possessed antipsychotic properties and produced symptomatic improvement in patients with schizophrenia. But, conventional anti-psychotics carry the risk of side

Table 2: Clinical characteristics of favourable vs. unfavourable groups (n= 100)

	Favourable (n = 49)	(%)	Unfavourable (n = 51)	(%)	p value
Duration of Symptoms					
< 6 months	35	71%	21	41%	.0004
> 6 months	14	29%	30	59%	
Type of Symptoms					
Positive only	18	37%	8	15%	
Negative only	2	4%	5	10%	ns
Both	29	59%	38	75%	
Family History of Mental Illness					
Present	25	51%	23	45%	ns
Absent	24	49%	28	55%	
Identified Stressor					
Present	33	67%	26	51%	ns
Absent	16	33%	25	49%	
Perpetuating Factor					
Present	14	29%	16	31%	ns
Absent	35	71%	35	69%	

effects (14) that contribute to treatment non-adherence leading to relapse and re-hospitalizations. Any effort to minimize the side effects by lowering the dose would risk decreased efficacy and relapse (15). However, this study did not specifically study the use of antipsychotics, its side effects and medication compliance to comment on the direct relationship of antipsychotics to the outcome. Further studies need to be done locally looking into the efficacy of typical and atypical antipsychotics in those subjects who develop schizophrenia at an early age.

In regards to the demography of the study subjects, there was almost equal number of males and females. Though it is well recognized that there is equal gender distribution in schizophrenia, this finding was unexpected as one would expect to find more males in a group of schizophrenics with an onset before the age of 18 as it is well documented that males have an earlier onset. Most of the subjects were single, and though it is easy to conclude that schizophrenics are more likely not to get married due to the devastating nature of their illness, we are unable to conclude this here as most of the patients can be considered too young to be married at the time of the interview.

Though about half of the study subjects had reported a positive family history of psychiatric illness, it was not significantly related to the outcome. However this figure is considered high compared to studies that show that 10% – 15 % of schizophrenics have a positive family history of mental illness (16). Could this mean that EOS is more likely to have family members with mental illness as compared to schizophrenics with a later onset? Certainly more and larger studies are needed to confirm this. Furthermore family history of psychiatric illness in the present study could be inaccurate and incomplete as the subjects very often did not know the precise diagnosis of the family psychiatric illnesses and just reported that psychiatric illness had occurred in the family.

More than half of the subjects had stressors before the onset of illness. The onset of psychosis is generally accepted as involving the impact of stress upon a biological predisposition. Stress vulnerability models that were applied to schizophrenia are equally applicable to early onset psychosis. One study reported preceding events like unhappy love life, drug or alcohol abuse, poor parental care, and parents' marital problem had occurred prior to the onset of psychosis (17). Obvious precipitating factor was one the predictors of good outcome of schizophrenia (1). However in this study the presence or absence of stressor was not significantly related to the outcome of the illness.

In regards to the social class in this study, 74% of them were from lower social class (Class IV and V) compared to 26% from upper social class (Class II and III) and none was reported from social class I, which is comparable with past studies (18,19). Though most of the patients in this study were from lower socio-economic group the outcome of their illness was not significantly related to their social class. At present, one can speculate that people from higher social class can afford atypical antipsychotics that may alter the outcome more positively. It would be beneficial to conduct similar studies in our local settings to assess the usefulness of atypical antipsychotics.

Being involved in some form of employment like working or studying was significantly related to the outcome of the illness. In this study, about three quarter of the subjects from the favourable group were either working or studying. Employment status therefore could give a rough idea about level of functioning and could be used as a simple assessment guide.

A significant number of subjects from the unfavourable group had delayed themselves in getting appropriate treatment from the psychiatric service of the hospital. Research suggests that the possibility of a more favourable outcome is possible, if effective treatment is initiated and maintained early in the course of the illness (20). Poor outcome that has typically been associated with an insidious onset of schizophrenia may result in delayed diagnosis and delayed use of antipsychotic medication (21). It is believed that the insidious onset in many early onset schizophrenics could be the prodromal phase (22) of the disease and intervention during this phase may help to prevent the onset of psychosis (23).The awareness of this devastating mental illness is rather poor in our country which contributes to delay in getting early professional help. Preventive intervention strategies for the prodrome include early recognition and access to services through increasing awareness of specific group like parents, teachers, school counselors, general practitioners and health professionals. Hence, case identification should be intensified so that

early interventions can be initiated to prevent possible disabilities.

A significant number of subjects from the unfavourable group had the onset of their illness at a very early age i.e. 15 years and below. Schizophrenia was once considered as a functional disorder but, now it is believed to be a brain disorder. Evidence show that prolonged untreated psychosis contributes to brain dysfunction as evidenced by smaller volumes of the superior temporal cortex (24). The outcome of the illness was found not to be significantly related to the type of presenting symptoms. Negative symptoms have been linked to poorer prognosis and poorer response to neuroleptics (25), while positive symptoms were associated with better prognosis (26, 27). The number of subjects who presented with negative symptoms alone in this study was too few to comment on the outcome. The psychotic symptoms at the first contact were based on the case notes, and there could be a possibility of incomplete documentation of the symptoms at the time of initial presentation.

Finally, certain limitations are recognized in this study. The presenting complaints and symptoms were based on the case records during the first contact. No scales were used for the assessment of positive and negative symptoms at the onset of illness as the initial symptoms were based on the case notes. The study did not examine the effects of any obstetrics complications that were likely to contribute to early psychosis. The study did not include the effects of the interventions like pharmacotherapy, psychotherapy or rehabilitation used in the study subjects.

In conclusion, this study revealed that those with a younger age of onset and those with a longer duration of presenting symptoms before their first contact, had a worse outcome. It was also found that subjects from the "favourable" outcome group were more likely to be either employed or studying. Based on these findings, it is recommended that mental health services should be expanded to provide services of early identification and intervention to minimize the duration of untreated psychosis and prevent poor outcomes. Extra focus should be paid on young adolescence as onset of schizophrenia during this period is associated with a worse outcome.

References

1. Carpenter WT, Buchanan RW. Schizophrenia [Review]. N Engl J Med 1994; 330: 681-690.

2. Kaplan H, Sadock B. Synopsis of Psychiatry. Baltimore: Lippincott Williams & Wilkins, 7th Edition. 1996: 46-472.

3. Volkmar FR, Cohen DJ, Hoshine Y, *et al.* Phenomenology and Classification of Childhood Psychosis. Psychological Medicine 1988; 18: 191-201.

4. Maziade M, Gingras N, Podrigue C, *et al.* Long Term Stability of Diagnosis and Symptoms Dimensions in Systematic Sample of Patients with Onset of Schizophrenia in Childhood and Early Adolescence. British Journal of Psychiatry 1996;169: 361-370.

5. Hafner H, Gattaz WF. Onset and Early Course of Schizophrenia in Causes of Schizophrenia. New York: Springer Publishers, 1995.

6. Lieberman JA, Fenton WS. Delayed Detection of Psychosis: Causes, Consequences and Effects on Public Health. American Journal Psychiatry 2000; 157: 1727-1730.

7. McGlashan T.Duration of Untreated Psychosis in First Episode Schizophrenia: Marker or Determinant of Course? Biological. Psychiatry 1999; 46: 899-907.

8. Pathmavathi R, Rajkumar S, Kumar N, *et al.* Schizophrenic Patients Who Were Never Treated: A Study in an Indian Urban Community. Psychol. Med 1998; 28:1113-1117.

9. Werry JS, McClellan JM., Chard I, *et al.* Childhood and Adolescent Schizophrenic, Bipolar, Schizoaffective Disorders. A Clinical Outcome Study. J Am Acad Child Adolesc Psychiatry 1991; 30: 457-465.

10. Hergarty JD, Baldessarini MD, Tohen M, *et al.* One Hundred Years of Schizophrenia: A Meta-analysis of Outcome Literature. American Journal Psychiatry 1994; 151: 1409-1415.

11. Vazquez Barquero JL, Cuesta MJ, Herrera Castanedo S, *et al.* Cantabria First Episode Schizophrenia Study: Three Year Follow Up. British Journal of Psychiatry 1999; 174: 141-149.

12. Maziade M, Gingras N, Podrigue C, *et al.* Long Term Stability of Diagnosis and Symptoms Dimensions in a Systematic Sample of Patients with Onset of Schizophrenia in Childhood and Early Adolescence I. British Journal of Psychiatry 1996; 169: 361-370.

13. Reid I. Social Class Differences in Britian. London: Fontana Press, 1989, 3rd. Edition: page; 116.

14. Kane JM. Tardive Dyskinesia: Epidemiological and Clinical Presentation. In: Bloom FE and Kupfer DJ (eds). Psychopharmacology: The Fourth Generation of Progress. New York: Raven Press, 1995: 1485-1495.

15. Dawkins K, Lieberman JA, Lebowitz BD, *et al.* Antipsychotics: Past and Future. Schizophrinia Bulletin 1998; 25: 395-405.

16. Keith H. Nuechterlein Annotation Childhood Precursor of Adult Schizophrenia. Journal of Child Psychology and Psychiatry 1986; 27 (2):133-144.

17. Bjorn RR. Fully Recovered Schizophrenics: A Retrospective Study of Some Premorbid and Treatment Factors. Psychiatry 1990; 53: 127-139.

18. Green W. Schizophrenia with Childhood Onset. A Phenomenological Study of 38 cases. Journal of Am Acad of Child and Adolescent Psychiatry 1992 :35, 968-976

19. Canton S. Childhood Schizophrenia Present But Not Accoutered For. American Journal of Psychiatry 1982; 89: 139-146.

20. Wyatt R. J. Neuroleptics and the natural course of schizophrenia. Schizophrenia Bulletin 1991; 17: 325-351.

21. Loebel AD, Lieberman JA, Alvir JMJ. Duration of Psychosis and Outcome in First-Episode Schizophrenia. American Journal of Psychiatry 1992; 149: 1183-1188.

22. Werry JS, McClellan JM. Predicting Out Come in Early Onset Schizophrenia and Bipolar Disorder. J Am Acad Child Adolescent Psychiatry 1992; 31(1): 147-150.

23. Mrazek PJ, Haggerty RJ. Reducing risk of Mental Disorders. Washington: National Academy Press, 1994.

24. Keshavan MS, Schooler NR, Sweeney JA, *et al.* Superior Temporal Gyrus and the course of Early Schizophrenia: Progressive, Static or Reversible? Journal of Psychiatric Research 1998; 32: (3-4); 161-167.