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Research Article

A clinical study of minor physical anomalies in patients with schizophrenia

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ABSTRACT

Background: Minor physical anomalies (MPA) are unusual morphological deviations that have no serious medical or cosmetic significance to an individual. But however minor they may be, various studies across the world have revealed their significance as a possible endophenotype of schizophrenia. This study is an attempt towards understanding the various sociodemographic and illness correlates as well as the prevalence of MPA in people with schizophrenia.
Methods: 100 admitted patients who fulfilled the criteria for schizophrenia as laid down by international classification of diseases version 10 (ICD-10) and other inclusion and exclusion criteria over one year period with age between 16-60 years were included in the study. A standardized semi structured proforma for various sociodemographic and illness variables and Waldrop minor congenital anomaly scale (weighted version) were applied on the study subjects. Data obtained was analyzed using SPSS and chi-square was applied to find out statistical association.
Results: Minor physical anomalies were found to be present in only 15% of subjects and they have a statistically significant association with age (p=0.041) and occupation (p=0.002).
Conclusions: The study of MPA in schizophrenia is a novel attempt to unearth any subtle associations between the genetic abnormality and its interactions with the various psychophysiological as well as other environmental factors which ultimately leads to the endophenotype and in some cases to the ultimate illness state. In our study the presence of MPA in 15% of the subjects with various degree of severity probably indicates heterogeneity of the schizophrenia illness and a complex interaction with various factors from genotype to phenotype.

Keywords: Schizophrenia, Endophenotype, Minor physical anomalies, Demographics

INTRODUCTION

"Schizophrenia is a clinical syndrome of variable, but profoundly disruptive psychopathology that involves cognition, emotion, perception, and other aspects of behaviour."[1] According to diagnostic and statistical manual 5th edition, the lifetime prevalence of schizophrenia is 0.3-0.7%.[2]

However, over the years, in the study of complex psychiatric diseases like schizophrenia, concept of certain measurable components have come up, that are apparently invisible to the naked eyes but bridges the gap between the distal genotype and the manifest disease like

endophenotypes. Gottesman & Shields in 1973[3] first adopted the term 'endophenotype' and proposed four criteria to define it. Those being "The endophenotype should be associated with illness in the population, should be heritable and primarily state-independent (manifests in an individual whether or not illness is active) and it should co-segregate with a psychiatric illness." Leboyer et al in 1998 suggested an additional criteria that endophenotype are found at a higher rate in the family members of the affected rather than those of unaffected.[4]

Minor physical anomalies (MPAs), as described by Jones[6] are "Unusual morphological deviations that have no serious medical or cosmetic significance to an individual", but however minor they may be, according to Hoyme et al,[7] they can be "a marker of abnormal environmental or genetic stress in the developing embryo" and hence can be considered as risk markers of an underlying disease.

Numerous in vivo neuroimaging studies have revealed compelling evidence of morphometric changes in the schizophrenia brain and many post-mortem studies have found replicable cellular and molecular abnormalities; however, none of the findings can be definitely attributed to a developmental origin. Here comes the significance of MPA as an endophenotype in schizophrenia as indirect evidence to the theory of neurodevelopmental origin. According to Tarrant et al[8] "Minor physical anomalies, a static marker of developmental disturbance, are also increased in schizophrenia". Murphy et al[9] on the other hand has commented that "At present, it is unclear if MPAs are directly related to the pathogenesis of the disorder" and has suggested the need of further studies for more data on this topic.

The present popular concept is that, people with these endophenotypes are having an inherent deficit and hence may develop the corresponding illness only if they are exposed to specific types of environmental stressors in a highly complex way.

This study of ours which has been conducted in the north eastern part of India, is a novel attempt towards understanding the prevalence, types and distributions of various 'Minor physical anomalies' in patients with schizophrenia and also to evaluate the underlying association between various MPA with different sociodemographic variables including few specific clinical variables in schizophrenia.

Aims and objectives

- To study the prevalence, types and distributions of minor physical anomalies in schizophrenia.
- To see the association of minor physical anomalies with socio-demographic and illness variables in patients with schizophrenia.

METHODS

This cross-sectional study was conducted at Lokopriya Gopinath Bordoloi Regional Institute of Mental Health (LGBRIMH), Tezpur, Assam a town in the north-eastern part of India in the year 2009-2010 after getting clearance from the hospital ethics committee. LGBRIMH is a tertiary care institute providing mental health facility to the whole of the north-east region of India. 100 patients from both sexes serially admitted in the inpatient ward diagnosed as a case of schizophrenia according to international classification of diseases version 10 (ICD-10) during the one year period with age between 16-60 years were included in the study. The patients with neurological disorders such as seizure disorder, movement disorders, cerebral palsy as evaluated by a detailed neurological examination, patients with recent or current medical illness that may impair central nervous system function, patients with any other psychiatric comorbidity or those with a life time history of head injury associated with loss of consciousness, seizures, neurological deficits, or surgical intervention were excluded from the study.

Tools

A semi structured proforma was designed for the study to collect and record information regarding socio-demographic data like age, gender, education, marital status, occupation and clinical variables like family history of schizophrenia, duration of illness, and handedness.

International classification of diseases (ICD - 10)

The tenth revision of the International Classification of Diseases by World Health Organization, Geneva (1992) was used. Patients who were diagnosed with schizophrenia as per the criteria of this manual were recruited into the study.

Waldrop minor congenital anomaly scale (Waldrop and Halverson 1971)

The standard instrument in assessing MPA is a scale developed by Waldrop and associates which standardizes the measurement of 18 different anomalies of the head, eyes, ears, mouth, hands and feet. This instrument for measurement of MPA has good test-retest reliability, inter-rater reliability and long term stability.[10] The content of Waldrop scale is highly relevant for the investigation of a developmental disorder like pervasive developmental disorder and schizophrenia. In most studies MPA score of 3 is considered as positive.

The scale can be used in two different ways

Unweighted: with items scored as either 1 (Present) or 0 (Absent), giving a maximum score of 18.

Weighted: with a few items scored on the basis of severity, as 0, 1, 2, giving a maximum score of 24. In weighted scoring system a few items are totally excluded and rated as 0. The weighted scoring system was developed to maximize the difference in score between the subjects with developmental disorders and normal subjects (Low MPA = 0-2; High MPA = more than 3).

Procedure

Patients admitted in the inpatient ward of LGBRIMH, Tezpur who were diagnosed with schizophrenia were assessed initially for the inclusion and exclusion criteria. With the criteria being fulfilled, the socio-demographic and clinical variables were collected in the pro forma. The waldrop minor congenital anomaly scale (Waldrop and Halverson 1971) were administered to the patient and data recorded in Microsoft Excel datasheets.

Informed consent was taken from the primary care giver and the patient.

Statistical analysis

The observed findings were analyzed by using Statistical Package for the Social Sciences (SPSS) software compatible with windows operating system. Descriptive statistics in terms of percentage were used for categorical variables. Chi square test was used where ever applicable. Pearson's coefficient correlation was evaluated for examining the relationship between variables specified. The results were compared with available literature in the area.

RESULTS

We found that, maximum subjects are between 20-39 years of age (69%) with a mean age of 32.02 years, male (69%), unmarried (61%), primary educated (45%) and unmarried (45%). Detailed sociodemographic data is shown is table 1. The duration of illness in most of the study subjects was found to be between 1-9 years (56%), 37% of subjects have a positive family history of schizophrenia and majority of the subjects are right handed, that is 89% (Table 2). Minor physical anomalies were present in only 15% of subjects, the total MPA score was 74, mean MPA score of total study subjects (n=100) was found to be 0.74±1.43 (Table 3).

The associations between MPA score and the sociodemographic variables are shown in Table 4. The maximum number of MPA was found in the age group 40-49 years, and the variation of score with age was found to be statistically significant (p=0.041; df =4). The frequency and number of MPA was more in males and in the married group. Maximum MPA score was found in the primary educated group, followed by the higher secondary group, however interestingly no anomaly was found in the illiterate group. We also found that the frequency of MPA was maximum in the cultivator group followed by the unemployed group. The difference was found to be statistically significant (p=0.002; df =7). MPA score was slightly higher in the group with family history of schizophrenia, though statistically not significant. No statistically significant correlation was observed between the MPA score and the duration of illness. It was also found that the MPA score was high in the mixed handed group and almost similar in the right and left handed group. However, this finding was not statistically significant.

Table 1: Sociodemographic data of study subjects.

Age	
Age in years	Number of subjects
<20	8
20- 29	35
30-39	34
40-49	18
>50	5
Sex	
Male	69
Female	31
Marital status	
Married	39
Unmarried	61
Widow/widower	0
Seperated/divorcee	0
Educational status	
Illiterate	8
Primary	45
High school	21
Higher secondary	13
Graduate and above	13
Occupation	
Unemployed	45
Daily wage earner	9
Cultivator	8
Business	7
Skilled worker	4
Service holder	5
Professional	7
House wife	15

Table 2: Data on illness variables of study subjects.

Variables	**Number of subjects**
Duration of illness in years	
<1	9
1-4	28
5-9	28
10-14	15
>15	20
Family history	
Positive	37
Negative	63
Handedness	
Right	89
Left	7
Mixed	4

Table 3: Distribution of MPA in the study subjects.

Score	Total (N)	MPA Positive (N)	Total Score	Mean Score	Standard deviation
MPA	100	15	74	0.74	1.43

Table 4: Distribution of the MPA positive subjects according to the severity of MPA score and its associations with socio-demographic & illness variables.

Variables	MPA score		df	p-value
	<3	>3		
Age in years				
<20	100%	0%	4	0.041
20-29	80%	20%		
30-39	94.1%	5.9%		
40-49	66.7%	33.3%		
>50	100%	0%		
Sex				
Male	81.2%	18.8%	1	0.109
Female	93.5%	6.5%		
Marital status				
Married	82.1%	17.9%	1	0.509
Unmarried	86.9%	13.1%		
Education				
Illiterate	100%	0%	4	0.145
Primary	75.6%	24.4%		
High school	95.2%	4.8%		
Higher secondary	84.6%	15.4%		
Graduate & above	92.3%	7.7%		
Occupation				
Unemployed	84.4%	15.6%	7	0.002
Daily wage earner	100%	0%		
Cultivator	37.5%	62.5%		
Business	85.7%	14.3%		
Professional	100%	0%		
Skilled worker	100%	0%		
Service holder	60%	40%		
Housewife	100%	0%		
Family history				
Positive	81.1%	18.9%	1	0.4
Negative	87.3%	12.7%		
Duration of illness				
<1 years	77.8%	22.2%	4	0.761
1-4 years	89.3%	10.7%		
5-9 years	89.3%	10.7%		
10-14 years	80%	20%		
>15 years	80%	20%		
Handedness				
Right	86.5%	13.5%	2	0.135
Left	85.7%	14.3%		
Mixed	50%	50%		

DISCUSSION

Our study is a hospital-based, cross-sectional study on serially taken 100 patients with schizophrenia to find out the prevalence and types of minor physical anomalies in schizophrenia and to evaluate the association of socio-demographic and illness variables with minor physical anomalies in patients with schizophrenia.

In our study the minor physical anomalies were found to be present in only 15% of subjects. This is similar to study done by McNeil et al which failed to show a higher rate of minor physical anomalies in schizophrenia patients.[10] They commented, "The inferred genetic risk for psychosis does not appear to be associated with greater rates of early somatic developmental anomalies, suggesting that early developmental anomalies do not represent an expression of genetic influence toward psychosis." However, in contrast to this statement, majority of studies showed an excess of minor physical anomalies in schizophrenia.[11-14] Gualtieri et al studied anomalies in 3 groups: chronic schizophrenics, alcoholic adults, and normal adults and reported that patients with schizophrenia were found to have significantly more anomalies than both normal and alcoholic adults.[13]

Similarly, a study done by Ismail et al, to assess the frequency and type of minor physical anomalies in patients with schizophrenia and their normal siblings, reported that 60% of patients and 38% of the siblings, but only 5% of the control subjects had a higher rate of minor physical anomalies.[15]

In another study done by Lohr et al, the Waldrop physical anomaly scale was used to assess the prevalence of minor physical anomalies in 3 groups: schizophrenic patients, patients with mood disorder, and normal controls.[16] Using the Kruskal-Wallis analysis of variance (ANOVA) and the Mann Whitney U test, patients with schizophrenia were found to have significantly more anomalies than controls ($p<0.003$).

Association between socio-demographic variables and MPA scores

Age

In our study, a significant association was found between age and the MPA score ($p=0.04$) (Table 4). No study has been found to report an association between age and the MPA score. In the study done by Lohr et al also found no association between MPA score and age.[16]

Gender

We found MPA score to be more in males; however, this finding is not statistically significant (Table 4).

Similar to our study, John et al in his study found no gender differences in the frequencies of MPA.[17] The

same finding has been reported in other studies done by Green et al[12] and McGrath et al,[18] but excess MPAs in male schizophrenia patients have been reported in a studies done by Marcus et al,[19] Sivkov and Akabaliev et al,[20] whereas excess MPAs in female schizophrenia patients have reported in a study done by Lal et al.[21]

Marital status

In our study we found that majority (61%) of the subjects were unmarried, and the reason for this might be the fact that more than 70% of subjects in our study were less than 40 years of age and in many of these subjects illness started in their 2nd or 3rd decade of life (Table 1). MPA score was found to be more or less equal in both the groups, and there was no significant difference statistically among the married and unmarried group (Table 4). We did not find any study which has compared the association between the MPA and marital status.

Education

In our study more than 40% subjects have studied up to primary school, and around 25% were those who have passed higher secondary or have done graduation or above (Table 1). No statistically significant association was found between MPA score and educational status in our study (Table 4). Similar to our study no association has been reported by any other studies conducted.[16,17]

Occupation

Regarding occupation, we found that more than 40% of patients were unemployed, and almost equal number of subjects was present in other categories. House wives comprised 15% of subjects (Table 1). The higher number of unemployed subjects is probably due to the fact that schizophrenia is a chronic illness with onset during adolescence, impairing acquisition of skills required for vocational achievement, and even many patients who were productive before onset becomes non-productive later as chronicity develops. MPA score was found to be maximum in the cultivator group followed by the daily wage earner group. The association between MPA score and occupation was found to be statistically significant (p=0.002) (Table 4).

But no studies have been found to report an association between MPA and occupational status and therefore the finding of our study could not be compared.

Association between MPA score and illness variables

Family history

In our study about 40% of subjects were those with a positive family history of schizophrenia (Table 2). Similarly MPA score was more in subjects with a positive family history but the difference was not statistically significant (Table 4).

Regarding MPA and family history, one research group examined MPAs in high-risk offspring of women with psychotic disorders and a control group of offspring of women with no history of psychosis, and found no difference in MPAs between the high-risk children and offspring of the control group.[22]

But, O'Callaghan et al found that MPAs in a group of 41 schizophrenia patients were related to a family history of schizophrenia as well as a history of obstetric complications, particularly bleeding in early pregnancy.[23]

Duration of illness

In our study around 60% of subjects were those with duration of illness of 1-10 years, and 20% subjects had illness for more than 15 years (Table 2). MPA score was not found to have any association with duration of illness (Table 4). Similarly duration of illness was not found to be associated with MPA in study done by John et al (2008).[17]

Handedness

90% of the patients in our study were right handed, and the rest 10% comprised of left handed and mixed handed subjects (Table 2). MPA score was found to be more in mixed handed subjects; however, no statistically significant association was found (Table 4).

Some studies reported an excess of mixed-handedness in patients with psychosis, and especially with schizophrenia.[22,24] Similar to the finding of our study, regarding MPA score and handedness, no association was reported in the study done by John et al (2008).[17]

CONCLUSION

This study is the first of its kind in this region where we made an attempt to see the prevalence of minor physical anomalies in schizophrenia patients and to see their association with socio-demographic and illness variables. Most of the subjects in our study were males (69%) between the age group 20-39 years, and majorities were unmarried (61%). Most of the subjects were primary school dropout (45%), and only a few were graduate and above (13%), with majority of them being unemployed (45%). Most of the subjects had a negative family history (63%), and were right handed (89%), with duration of illness between 1-10 years (56%). In our study we found, only 15% of the subjects with schizophrenia have MPA, which is significantly more than general population. Probably it indicates a group of patients with schizophrenia who are having the genotype of MPA interacting with favorable environmental variables and finally expressing as an endophenotype, which indicates the heterogenic nature of the illness. We found that MPA have a statistically significant association with age and occupation.

However this study also has its limitations. This being a hospital based study; the result may not reflect the exact picture of the community. Another limitation was that no control group was selected. More over the sample size was small; therefore it's difficult to generalize the result. The subjects were not followed up to detect any changes in minor physical anomalies over time.

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