e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(8); 503-510

Original Research Article

Study of Minor Physical Anomalies in Schizophrenic Patients: A Case Control Study

Swapanjit Sarma[1], Bhaktishree Raha[2], Nilanjan Chandra[3], Dhrubjyoti Bagchi[4], H.R. Phookun[5]

[1,2,3]Assistant Professor, Department of Psychiatry, ICARE Institute of Medical Sciences & Research, Balughata, Haldia 721645, West Bengal, India

[4]Associate Professor, Department of Psychiatry, ICARE Institute of Medical Sciences & Research, Balughata, Haldia 721645, West Bengal, India

[5]Professor and Head, Department of Psychiatry, Gauhati Medical College, Guwahati 781032, Assam, India

Received: 25-05-2024 / Revised: 23-06-2024 / Accepted: 26-07-2024

Corresponding Author: Dr. Dhrubjyoti Bagchi

Conflict of interest: Nil

Abstract:

Background: This study was undertaken to determine the prevalence of Minor Physical Anomalies in Schizophrenic patients and to compare that with normal healthy controls.

Materials & Methods: The study sample comprises of 50 consecutively selected subjects admitted in the Department of Psychiatry, Guwahati Medical College and Hospital and diagnosed as having schizophrenia and meeting the selection criteria. This study aimed to compare prevalence of minor physical anomalies in schizophrenics and normal healthy population. Semi-structured interview schedule for collection of socio-demographic data was captured. ICD–10 criteria were used for the diagnosis of schizophrenia and WALDROP Scale for assessment of minor physical anomalies.

Results: Schizophrenic patients have significantly more minor physical anomalies than normal controls in head circumference ($p = 0.0070$), hypertelorism ($p<0.0001$), low set ears ($p<0.0001$), high steepled palate ($p<0.0001$) and longer 3rd toe than 2nd ($p = 0.0078$). The analysis is further extended in to see if these items have specificity in discriminating schizophrenics from normal controls. Using Fisher's exact test, P values, sensitivity and specificity of these individual Waldrop items are calculated.

Conclusion: Male and female schizophrenic patients didn't differ regarding mean total anomaly score. Schizophrenic subjects had significantly more Minor Physical Anomalies than normal controls. Wider head circumference, hypertelorism, low set ears, high-steepled palate and 3rd toe longer than second had significantly higher prevalence in schizophrenic patients, and also predicted schizophrenic status with adequate sensitivity and specificity. Early onset schizophrenia cases had significantly more anomalies than late onset cases.

Keywords: Schizophrenia, Minor Physical Anomalies (MPAs), WALDROP Scale, Case Control Study.

Introduction

The complexity and heterogeneity of schizophrenia means that even its definition and diagnostic criteria are cause for debate, therefore the search for a satisfactory etiological theory of this condition would always be challenging. The genetic component of schizophrenia is undeniable given that having a schizophrenic relative is the biggest risk factor for schizophrenia. However, the fact that the monozygotic twin of a schizophrenic patient has only a 48 percent chance of developing the disease implies that other factors must be involved.[1] Biochemical theories focus on the possibility that localized excesses of one or more neurotransmitters, notably dopamine and serotonin, may account for the symptoms experienced in schizophrenia and the therapeutic effect of neuroleptics blocking these receptors reinforces this idea. [2] Schizophrenia is clearly a multifactorial disorder, including both genetic and environmental factors. Clinical studies using risk assessments have identified some relevant factors, including prenatal and birth complications (hypoxia, infection and substance/toxicant exposure), family history, body dysmorphia, and presence of mild premorbid deficits in social, motor and cognitive functions. [3] To explain the long lag between prenatal brain insult and late teen development of schizophrenia, 2 models of neurodevelopmental abnormalities are given – the early neurodevelopmental model and the late neurodevelopmental model. The early model is based on the view that a fixed lesion from early life

interacts with normal neurodevelopment occurring later, lying dormant until the brain matures sufficiently to call into operation the damaged systems. [4] The late developmental model proposes that schizophrenia may develop from aberrant or excessive periadolescent "synaptic pruning". [5] During early fetal development, cerebral and craniofacial morphogenesis is closely related and share a common ectodermic origin.

Morphologic anomalies can range from very severe (which are probably produced in earlier stages of development) to MPAs. These anomalies are markers of abnormalities in organogenesis at the end of the first trimester and beginning of the second trimester of gestation. [6

Since the early study by Goldfarb and Botstein in 1976, many investigators have convincingly demonstrated the increased prevalence of minor physical anomalies in schizophrenic patients in comparison to healthy controls and their biological relatives. At least 12 different studies have found increased rates of MPAs in adults with schizophrenia, [7] whereas one study failed to find a significant increase in patients [8].

Recent Indian study examining MPAs has shown significantly increased prevalence of MPAs in antipsychotic-naïve, first-episode schizophrenia patients in comparison to age, sex, education and socioeconomic status matched healthy control subjects. [9]

The present study will be the first of its kind from this institution and in this study, the construct of MPAs as a stable and early endophenotype of schizophrenia will be evaluated. This study intends to find if schizophrenics really manifest more MPAs in comparison to healthy controls and is there any predictive value of the MPA construct in guiding early detection of schizophrenic risk and subsequent preventive measures.

Materials and Methods

This cross-sectional, case-control study has been conducted in the Department of Psychiatry, Guwahati Medical College and Hospital, Guwahati. The study sample comprises of 50 consecutively selected subjects admitted in the Department of Psychiatry, Guwahati Medical College and Hospital and diagnosed as having schizophrenia and meeting the selection criteria. The diagnosis of schizophrenia was made using the "International Classification of Diseases (ICD-10) for Mental and Behavioral Disorders".

Aims and Objectives:

1. To compare the prevalence of minor physical anomalies between schizophrenic patients and normal controls.
2. To compare the prevalence of minor physical anomalies between male and female schizophrenic patients.
3. To compare the regional distribution of individual anomalies between schizophrenic patients and normal controls.

Inclusion Criteria:

1. Diagnosed cases of schizophrenia according to ICD– 10, irrespective of duration and subtype of schizophrenia
2. Sex – both male and female patients
3. Age group – 14 years and above

Exclusion Criteria:

1. Patients with co-morbid major psychiatric illness.
2. Schizophrenic patients with obvious mental retardation
3. Patients suffering from any co-morbid serious medical illness
4. Patients with any identifiable neurological disorder (seizure disorder, head injury, multiple sclerosis etc.)

The control group consists of 50 healthy relatives of non-schizophrenic patients selected from the Department of Psychiatry. Relatives of schizophrenic patients were not included in the study as extensive literature had established prevalence of increased rates of minor physical anomalies in biological relatives of schizophrenia; this study aims to compare prevalence of minor physical anomalies in schizophrenics and normal healthy population.

Tools for assessment:

1. Semi-structured interview schedule for collection of socio-demographic data
2. ICD–10 criteria for diagnosis of Schizophrenia
3. WALDROP Scale for assessment of minor physical anomalies

WALDROP Scale for Minor Physical Anomalies

The modified Waldrop and Halverson (1971)[10] scale focused on anomalies in the area of the head, eyes, ears, mouth, hand, and feet. This WALDROP scale contains 18 items scored in a graded manner.

This original WALDROP scale assigned 2 points for head circumference and inter-canthal distance abnormalities if these measurements vary from same sexed mean by more than 1.5 standard deviations and 1 point if variation is within 1 to 1.5 standard deviations.

A tape measure is used for head circumference and inter-canthal distance anomalies, others are inspected visually. Fine electric hair, epicanthus of eyes covered, low set ear, adherent ear lobes, high-sleepled palate, curved 5th finger and longer 3rd toe

than second are scored either 1 or 2 depending on set criteria for degree of deformity. Other items are simply scored 1 if the anomaly is reliably detected.

After selecting cases and controls as per selection criteria, an informed consent for participation in the study was taken from all patients and control subjects. Subjects were explained about the purpose of the study. Time period for interview ranged from 30-45 minutes including the WALDRROP scale. The data were analyzed by the following statistical procedures wherever applicable: Chi– square test, unpaired– t test and Fisher's Exact test.

Results

Table 1: Distribution of age among study groups

Age (year)	Cases (N=50)			Controls (N=50)		
	No	%	Mean age	No	%	Mean age
14 – 25	18	36	29.2 yrs	16	32	30.9 yrs
26 – 35	23	46		26	52	
36 – 45	7	14		5	10	
46 - 55	2	4		3	6	
>55	0	0		0	0	

The Table 1 shows that in the case group, 36% cases are aged 14 to 25 years, 46% aged 26 to 35 years, 14% aged 36 to 45 years and 4% aged 46 to 55 years.
Controls have 32% aged 14 to 25 years, 52% aged 26 to 35 years, 10% aged 36 to 45 years and 6% aged 46 to 55 years. Neither cases nor control group have any participant ageing more than 55 years. Mean age in cases is 29.2 years and that of controls is 30.9 years. [Chi-square 0.3601, df=2, P=0.8352] So, cases and controls are matched in relation to age categories.

Table 2: Distribution of sex among study groups

Sex	Cases (N = 50)		Controls (N = 50)		Total (N = 100)
	No	%	No	%	
Male	26	52	25	50	51
Female	24	48	25	50	49

Table 2 shows sex distribution in cases and controls. Cases comprised of 52% males and 48% females, while controls have 50% each of males and females. [Chi square = 0.04002, df=1, p = 0.8414, so cases and controls are matched in sex.]

Comparison of Total Waldrop Anomaly Scores between Cases and Controls

Table 3: Association of gender with WALDROP mean values

Study groups	Total Waldrop Anomaly Score						P value (t-test)
	Male			Female			
	Mean	95% C.I	S.D	Mean	95% C.I	S.D	
Case	6.65	5.93 – 7.37	1.79	6.08	5.35 – 6.80	1.72	0.2563
Control	1.80	1.22 – 2.38	1.41	1.72	1.13 – 2.31	1.43	0.8432

Table 3 shows that mean WALDROP scores doesn't differ in males and females. For cases, male vs. female, P = 0.02563; for controls, male vs. female P = 0.8432.

Table 4: Comparison between study groups with male and female combined

Study groups	Total Waldrop Anomaly Score			
	Mean	95% CI	S.D	P value
Cases	6.38	5.88 – 6.88	1.760	<0.0001
Controls	1.76	1.36 – 2.16	1.408	

Unpaired t – test: t = 14.495, df = 98

The two tailed p value: P < 0.0001, considered extremely significant. So, cases and controls show statistically significant difference in Total WALDROP Anomaly Score mean values.

Table 5: Waldrop Scale: Distribution of anomalies in subjects

Waldrop Items	Cases (N = 50)	Controls (N = 50)

	Male (N = 26)		Female (N = 24)		Male (N=25)		Female (N = 25)	
	No	%	No	%	No	%	No	%
Head:								
1. Fine electric hair	5	**19.2**	2	**8.3**	1	**4**	1	**4**
- Grade 1 ……..	5	**19.2**	4	**16.6**	-	**-**	5	**20**
- Grade 2 ……..	9	**34.6**	8	**33.3**	5	**20**	2	**8**
2. Two or more hair whorls…….	5	**19.2**	4	**16.6**	-	**-**	5	
3. Head circumference	9	**34.6**	8	**33.3**	5	**20**	2	
- > 1 SD – 1.5 SD…. …								
- > 1.5 SD ……								
Eyes:								
4. Epicanthus of eyes								
- Partial coverage …….	2	**7.7**	-	**-**	-	**-**	-	**-**
- Total coverage ……..	-	**-**	-	**-**	-	**-**	-	**-**
5. Hypertelorism								
- >1 SD – 1.5 SD …….	2	**7.7**	1	**4.1**	3	**12**	1	**4**
- >1.5 SD……..	15	**57.7**	14	**58.3**	2	**8**	2	**8**
EARS:								
6. Low seated ears								
- Grade 1 ……..	13	**50**	10	**41.6**	4	**16**	6	**24**
- Grade 2 ……..								
	6	**23**	9	**37.5**	1	**4**	-	**-**
7. Adherent ear lobes								
- Grade 1 ……..	5	**19.2**	5	**20.8**	7	**28**	2	**8**
- Grade 2 ……..								
	3	**11.5**	2	**8.3**	-	**-**	-	**-**
8. Malformed ears ……								
	1	**3.8**	1	**4.1**	-	**-**	-	**-**
9. Asymmetrical ears ……..								
	3	**11.5**	3	**12.5**	-	**-**	1	**4**
10. Soft and pliable ears ……...	3	**11.5**	2	**8.3**	-	**-**	1	**4**

From the above table 5, it is evident that schizophrenic patients have much higher incidence of all the individual anomalies in comparison to normal controls. No schizophrenic subjects as well as normal controls have anomalies of fine electric hair, tongue with smooth rough spots or single transverse palmer crease. Also, one interesting observation is that lower degrees of anomalies in head circumference, hypertelorism, adherent ear lobes and high-steepled palate are found more in normal controls. Head circumference grade 1 anomaly in females= 16.6% (cases) vs. 20% (controls); hypertelorism grade 1 anomaly in males = 7.7% (cases) vs. 12% (controls); adherent ear lobes grade 1 anomaly in males = 19.2% (cases) vs. 28% (controls); high-steepled palate grade 1 anomaly in males = 23% (cases) vs. 32% (controls) and in females = 20.8% (cases) vs. 28% (controls). It implies that schizophrenic patients not only have more prevalent anomalies than normal population, but also have higher degrees of malformations than controls. The above analysis showed that, schizophrenic patients have significantly more minor physical anomalies than normal controls in head circumference ($p = 0.0070$), hypertelorism ($p<0.0001$), low set ears ($p<0.0001$), high steepled palate ($p<0.0001$) and longer 3rd toe than 2nd ($p = 0.0078$). The analysis is further extended in to see if these items have specificity in discriminating schizophrenics from normal controls. Using Fisher's exact test, P values, sensitivity and specificity of these individual Waldrop items are calculated.

Table 6:

Discriminative analysis of each WALDROP items

Individual items	P value	Sensitivity	Specificity
Head circumference	0.0070	0.68	0.61
Hypertelorism	<0.0001	0.80	0.70
Low set ears	<0.0001	0.77	0.76
High-steepled palate	<0.0001	0.70	0.84
3rd toe longer than second	0.0078	0.91	0.55

Table 5 shows the discriminative analysis of individual WALDROP Anomaly items. From the above analysis, it is seen that longer 3rd toe has the highest sensitivity (91%) and high-steepled palate has the highest specificity (84%) for schizophrenic case status.

Relationship between Age at Onset and Minor Physical Anomalies

Table 7: Relationship between age at onset and MPAs

Age groups	Total Waldrop Anomaly Scores			
	Mean	S.D	95% CI	Unpaired t- test P value
18 year or less (EOS)	6.676	1.387	6.192 – 7.161	0.044
19 year or more (LOS)	5.684	2.110	4.667 – 6.701	

Table 7 shows the relationship between age at onset and MPAs. Subjects are divided into 2 groups – early (18 years or less) and late (19 years or more) age at onset. There are 31 patients in the early onset group and 19 patients in the late onset group. It is observed that the Early onset schizophrenia (EOS) and the Late onset schizophrenia (LOS) groups differ statistically significantly in terms of mean anomaly score; t = 2.065, df = 51, p = 0.044.

Table 8: Relationship of age at onset and prevalent anomaly

Waldrop Anomaly Score of Patients		
	<5	□5
EOS (18 or less)	1	30
LOS (19 or more)	5	14

Now, to refine the previous analysis of Table 8, schizophrenic subjects are further divided into 2 groups based on "prevalent anomaly".

Subjects who have an anomaly score of greater than 2 SDs above the mean for normal controls are considered as having "prevalent anomaly". This amount to [1.76 + 2(1.408)] = 4.6. So, subjects having anomaly score of 5 or more are considered to have prevalent anomaly. [Chi – square = 3.962, df = 1, P = 0.0465] So, it is seen that the early onset group has more prevalent anomalies than the late onset group.

Table 9: Discriminating value of total Waldrop Anomaly scores

Discriminating value of total Waldrop Anomaly scores							
MPA Total score	Case (N=50)	Control (N=50)	P value Chi-sq.	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
MPA-T □1	50	39	0.0014	100.0	22.0	56.2	100.0
MPA-T □2	50	26	<0.0001	100.0	48.0	65.8	100.0
MPA-T □3	49	14	<0.0001	98.0	72.0	77.8	97.3
MPA-T □4	47	8	<0.0001	94.0	84.0	85.4	93.3
MPA-T □5	44	1	<0.0001	88.0	98.0	97.8	89.0
MPA-T □6	34	0	<0.0001	68.0	100.0	100.0	75.8
MPA-T □7	24	0	<0.0001	48.0	100.0	100.0	65.8
MPA-T □8	14	0	0.0002	28.0	100.0	100.0	58.1
MPA-T □9	6	0	0.0353	12.0	100.0	100.0	53.2

Discussion

Gender: Analysis of the socio-demographic data in the study showed that the study group comprised of 52% male and 48% female schizophrenic patients compared with 50% each of controls, who were chosen to match for the sex distribution of case group.

This equal distribution of gender in study groups was reflective of the effort to eliminate the influence of gender bias. Gender bias is important as in the study by M. F. Green et al. 1989) [11], they have advised cautious interpretation of their result as the female cases were significantly less in comparison to males.

Age distribution: In this study, mean age in cases is 29.2 years and that of controls is 30.9 years. The study groups were matched in age (P = 0.8352).

Mean age of this study population was similar to the study done by J. P. John, V. Arunachalam et al. in 2008 in NIMHANS, Bangalore [12] where the mean age of cases was 30.03 year and that of controls was 30.77 years. Study by S. T. Sivkov and V. H. Akabaliev in 2003 [13] reported slightly higher mean age of 31.27 and 39.24 in cases and controls respectively.

Comparison of total Waldrop Anomaly scores between cases and controls

Differential influence of gender over Mean Anomaly Score: The primary outcome measure of this present study is the total anomaly score on the Waldrop Scale for Minor Physical Anomalies. The total score reflects the number and severity of different anomalies appearing in a particular case of schizophrenia that may point towards a developmental insult early in the embryogenesis (Waddington JL. 1999). [6] The mean score of total anomalies in the two study groups were compared. In the schizophrenic group, males had mean score of 6.65 (S.D 1.79) and females 6.08 (S.D 1.72), P = 0.2563, the difference considered to be non-significant. Similarly, in the control group, male and female comparison with regard to total anomaly score came out to be non-significant [1.80 (S.D 1.72) in males and 1.72 (S.D 1.43) in females, P = 0.8432].

In the study by M.F.Green, P. Satz et al. in 1989 [11], authors reported similar result regarding gender influence; they had also found similar prevalence of mean anomaly in male and females. However, they had found increased prevalence of anomaly in female schizophrenics in comparison to males [2.57 (S.D 1.40) for females vs. 1.81 (1.63) for male schizophrenics]. Their finding of this higher incidence in females however should be interpreted cautiously as the numbers of female schizophrenics were very small relative to males (53 men and 14 women). The only study that had found increased prevalence of anomalies in females was the early Indian study by Rakesh Lal and Shridhar Sharma in 1987 [14] had found significantly increased rate of anomalies in female patients [7.48 (S.D 2.06) in females vs. 6.46 (S.D 1.93) in males, P <0.05].

Comparison of total anomaly score in cases and controls: This study found out mean anomaly score in schizophrenics to be 6.38 (S.D 1.76) and that in controls 1.76 (S.D 1.408). This high prevalence of anomalies is statistically very significant, P <0.0001. At least 12 different studies found increased rates of MPA in schizophrenics (Ismail B, Cantor-Graae E, McNeil TF. 1998) [7] while one study failed to find statistically significant increase in schizophrenics in comparison to normal population (Alexander RC, Mukerjee S et al. 1994) [8].

Almost all the studies previously done to assess MPAs, Waldrop scale or its some form of modification were used. The findings of this present study is similar to the most recent Indian study by J. P. John, V. Arunachalam et al. 2008 in NIMHANS [12], Bangalore where they found that Schizophrenic subjects had significantly higher total MWS scores when compared to controls (p<0.001).

Bodily distribution of individual anomalies: From the present study, it is evident that schizophrenic patients have much higher incidence of all the individual anomalies in comparison to normal controls. No schizophrenic subjects as well as normal controls have anomalies of fine electric hair, tongue with smooth rough spots or single transverse palmer crease. Schizophrenic patients had significantly more minor physical anomalies than normal controls in head circumference (p=0.0070), hypertelorism (p<0.0001), low set ears (p<0.0001), high steepled palate (p<0.0001) and longer 3rd toe than 2nd (p=0.0078).

A discriminative analysis was done in this study to find out the sensitivity and specificity of different individual anomalies in predicting case status. It was seen that longer 3rd toe has the highest sensitivity (91%) and high-steepled palate has the highest specificity (84%) for schizophrenic case status. In the study by M.F.Green, P. Satz et al. 1989 [11], male patients showed a high incidence of abnormalities of the mouth compared to the normal controls. Although the female patients also showed a high incidence of mouth abnormalities, the most impressive finding for women was the high incidence of deviations in head circumference.

Relationship of age at onset and MPA: In this study, subjects were divided into 2 groups – early (18 years or less) and late (19 years or more) age at onset. There are 31 patients in the early onset group and 19 patients in the late onset group. It was observed that the Early Onset Schizophrenia (EOS) and the Late Onset Schizophrenia (LOS) groups differ statistically significantly in terms of mean anomaly score; t = 2.065, df = 51, p= 0.044. A further analysis on the basis of prevalent anomaly found out that the early onset group has more prevalent anomalies than the late onset group (chi-squared= 3.962, P= 0.0465).

The findings of the present study was similar to the study done by M.F.Green, P. Satz in 1989 [11], where they have also found significantly more MPAs in early onset schizophrenia group (P <0.05). Hata K, Iida J, Iwasaka H et al. 2003 [15] in their study also found significantly increased anomaly in EOS (early onset schizophrenia group)

than LOS (late onset schizophrenia group). The mean total Waldrop score was 3.92 (SD 1.86) in the EOS group, significantly higher than the 2.59 (SD 1.79) in the LOS group ($p < 0.05$).

Discriminating value of total Waldrop Anomaly score between schizophrenic patients and normal controls: In the present study, in schizophrenia patients there was no case scoring 0, MPA-T ranged from 2 to 10, and 28 percent had MPA-T ≥ 8. In normal controls, MPA-T ranged from 0 to 5, and only 2 percent had MPA–T≥ 5.

The discriminating effect of MPA-T for schizophrenia patient versus normal control status was assessed by comparing the groups for each step of MPA hierarchical scoring. The highest values of statistical significance were found for MPA-T ≥ 4 (chi-square = 58.34, df = 1) and MPA-T ≥ 5 (chi-square = 71.27, df = 1), indicating that they were best at discriminating between schizophrenia patients and normal controls.

MPA-T ≥ 4 had 94% sensitivity, 93.3% negative predictive value and 85.4% positive predictive value for detecting schizophrenia, while MPA-T ≥ 5 had 98% specificity and 97.8% positive predictive value. Analysis of the four test values trends (sensitivity, specificity, positive predictive value and negative predictive value) show that the cutoff scores that optimally discriminate schizophrenia patients from normal controls (having the most balanced sets of sensitivity, specificity, and positive and negative predictive values) are MPA-T ≥ 4 and MPA-T ≥ 5.

The present study finding corroborates with Stefan T. Sivkov and Valentin H. Akabaliev (2004) [13], who found the highest values of statistical significance for MPA-T ≥ 4 ($\chi 2 = 34.87$) and MPA-T ≥ 5 ($\chi 2 = 30.78$), indicating that they were best at discriminating between schizophrenia patients and normal controls. Thus, MPA-T ≥ 4 and ≥ 5 define the "border zone," where schizophrenia patients begin to prevail sufficiently and definitely over normal controls, although some normal controls still present with these MPA-T values.

Conclusion

The following findings can be concluded from the study: Maximum numbers of patients (46%) were in the age group of 26-35 years. Male and female schizophrenic patients didn't differ regarding mean total anomaly score. Schizophrenic subjects had significantly more Minor Physical Anomalies than normal controls. Wider head circumference, hypertelorism, low set ears, high-steepled palate and 3rd toe longer than second had significantly higher prevalence in schizophrenic patients, and also predicted schizophrenic status with adequate sensitivity and specificity. Early onset schizophrenia cases had significantly more anomalies than late onset cases. Total Anomaly score of ≥ 4 and ≥ 5 had highest discriminative value for prediction of schizophrenic case status.

Limitations of the study

- The sample taken was small; a large sample would have been more representative.
- The study population consisted only of admitted indoor patients. So, the results could not be projected to the general population.
- Maternal complications during early pregnancy and delivery, birth trauma etc. were not studied, which had robust research evidence in relating development of MPA and neurodevelopmental hypothesis of schizophrenia.

Take Home Messages: The findings of this study needs to be corroborated in a larger community sample representative of the whole population of the Indian setup. As studies concentrating on minor physical anomalies are very scarce in Indian setup, this study puts a much needed emphasis on further evaluating the neurodevelopmental hypothesis of schizophrenia.

The evaluation of minor physical anomalies is very informative as observed from the current study. It is an inexpensive and time efficient method to screen for early neurodevelopmental insult related to pathogenesis of schizophrenia. Further research can provide useful corroborating evidence in favor of using minor physical anomalies as an early screening tool for schizophrenia even before its development and guide preventive measures.

Ethical Approval: This study was approved by the Institutional Ethics Committee of Guwahati Medical College Ref. No.MC/2011/RP. 11/223, Dated 21.09.2011.

References

1. McGue M, Gottesman II. The genetic epidemiology of schizophrenia and the design of linkage studies. Eur Arch Psychiatry Clin Neurosci. 1991; 240(3):174-81.
2. Patel KR, Cherian J, Gohil K, Atkinson D. Schizophrenia: overview and treatment options. P T. 2014 Sep;39(9):638-45.
3. Salleh MR. The genetics of schizophrenia. Malays J Med Sci. 2004 Jul; 11(2):3-11.
4. Murray RM, Lewis SW. Is schizophrenia a neurodevelopmental disorder? Br Med J (Clin Res Ed). 1987 Sep 19; 295(6600):681-2.
5. Feinberg I. Schizophrenia: caused by a fault in programmed synaptic elimination during adolescence? J Psychiatr Res. 1982-1983; 17(4):319-34.
6. Waddington JL, Lane A, Scully PJ, Larkin C, O'Callaghan E. Neurodevelopmental and neuroprogressive processes in schizophrenia. Anti-

thetical or complementary, over a lifetime trajectory of disease? Psychiatr Clin North Am. 1998 Mar; 21(1):123-49.
7. Ismail B, Cantor-Graae E, McNeil TF. Minor physical anomalies in schizophrenic patients and their siblings. Am J Psychiatry. 1998 Dec; 155(12):1695-702.
8. Alexander RC, Mukherjee S, Richter J, Kaufmann CA. Minor physical anomalies in schizophrenia. J. Nerv. Ment. Dis. 1994; 182(11): 639–644.
9. Venkatasubramanian G. Schizophrenia is a disorder of aberrant neurodevelopment: A synthesis of evidence from clinical and structural, functional and neurochemical brain imaging studies. Indian J Psychiatry. 2007 Oct; 49(4):244-9.
10. Waldrop MF, Halverson, C. F. Minor physical anomalies and hyperactive behaviour in young children. In: Hellmuth J, edr. The exceptional infant. New York: Brunner/Mazel Publisher 1971;2:343-380
11. Green MF, Satz P, Christenson C. Minor physical anomalies in schizophrenia patients, bipolar patients, and their siblings. Schizophr Bull. 1994; 20(3):433-40.
12. John JP, Arunachalam V, Ratnam B, Isaac MK. Expanding the schizophrenia phenotype: a composite evaluation of neurodevelopmental markers. Compr. Psychiatry. 2008; 49(1):78–86.
13. Sivkov ST, Akabaliev VH. Minor physical anomalies in mentally healthy subjects: Internal consistency of the Waldrop Physical Anomaly Scale. Am. J. Hum. Biol. 2003; 15(1):61–67.
14. Lal R, Sharma S. Minor physical anomalies in schizophrenia. Indian J Psychiatry. 1987 Apr; 29(2):119-22.
15. Hata K, Iida J, Iwasaka H, Negoro HI, Ueda F, Kishimoto T. Minor physical anomalies in childhood and adolescent onset schizophrenia. Psychiatry Clin Neurosci. 2003 Feb; 57(1):17-21.