MINOR PHYSICAL ANOMALIES IN POSITIVE VERSUS NEGATIVE SYMPTOMS PATIENTS OF SCHIZOPHRENIA

Sneh Babhulkar[1], Durva B. Sail[2]

[1]Assistant Professor, Department of Psychiatry, B. J. Government Medical College and Sassoon General Hospital, Pune, Maharashtra.
[2]Resident Doctor, Department of Psychiatry, B. J. Government Medical College and Sassoon General Hospital, Pune, Maharashtra.

ABSTRACT

BACKGROUND

The term 'Minor Physical Anomalies (MPAs)' has been described by Jones (1988)[78] as "unusual morphologic features that are of no serious medical or cosmetic consequences to the patient. The value of their diagnosis is that they may serve as indicators of altered morphogenesis in a general sense or may constitute valuable clues in the diagnosis of a specific pattern of malformation."

The study was designed to examine the Minor Physical Anomalies in positive versus negative subsets of schizophrenic patients and identify the degree of abnormalities of this specific endophenotype and for understanding the association between various socio demographic and illness variables (like age, gender, duration of illness, handedness) between the subsets of schizophrenic patients.

MATERIALS AND METHODS

30 patients with positive symptoms of schizophrenia, 30 schizophrenic patients with negative symptoms and 60 age and sex matched controls were recruited from Psychiatry OPD and IPD from a tertiary care hospital. The Waldrop Minor Congenital Anomaly Scale (Waldrop and Halverson 1971) was applied for recording the scores of Minor Physical Anomalies.

RESULTS

The Minor Physical Anomaly (MPA) scores were significantly more in positive as well as negative subsets of schizophrenic patients with a statistical difference of ($p<0.0001$) as compared to healthy controls. However, there was no statistically significant difference in MPA scores between the two groups of schizophrenics.

CONCLUSION

Increased MPA scores in schizophrenic patients in comparison to controls advocate that Minor Physical Anomalies may be considered as a useful neuroendophenotypic marker for establishing an aetiopathogenesis in the schizophrenic disease process.

KEYWORDS

Schizophrenia, Positive and Negative Symptoms.

HOW TO CITE THIS ARTICLE: Babhulkar S, Sail DB. Minor physical anomalies in positive versus negative symptoms patients of schizophrenia. J. Evid. Based Med. Healthc. 2018; 5(47), 3266-3271. DOI: 10.18410/jebmh/2018/664

BACKGROUND

From neurodevelopmental perspective, central nervous system develops from the neuroectoderm; therefore the presence of minor physical anomalies may signal abnormal development of central nervous system.[1] Migration of the ectodermal cells of the foetal upper limb is simultaneous with neuronal migration to the cortex.[2] In a study of monozygotic twins discordant for schizophrenia, Bracha et al[3] reported that the affected co-twins had significantly higher total scores of fourth and fifth month dysmorphological hand anomalies compared with non-affected co-twins, implicating a second trimester insult. Other researchers (like O'Callaghan et al),[4] Mednick et al[5] reported higher frequency of bleeding during first trimester of pregnancy and high prevalence of viral infection in second trimester respectively with subsequent development of schizophrenia. The increased prevalence of minor physical anomalies may reflect the operation of common aberrant genes responsible for disordered neurodevelopment in schizophrenia which is also evident by its higher prevalence seen in intellectual disabilities and many neurodevelopmental syndromes. However, it is not clear in most studies on minor physical anomalies which anomaly has highest concordance/ correlation with positive or negative subsets of schizophrenia. Taking into account, the relative absence of studies having any correlation between, Minor physical anomalies specifically with Negative and Positive symptoms of schizophrenia we aim to evaluate and identify any obvious or occult presence of Minor Physical Anomalies in patients of schizophrenia with reference to their positive or negative symptom of schizophrenia.

Financial or Other, Competing Interest: None.
Submission 04-10-2018, Peer Review 11-10-2018,
Acceptance 02-11-2018, Published 14-11-2018.
Corresponding Author:
Dr. Sneh Babhulkar,
Department of Psychiatry,
B. J. Government Medical College and Sassoon General Hospital,
Pune- 411001, Maharashtra.
E-mail: snehbabhulkar@gmail.com
DOI: 10.18410/jebmh/2018/664

MATERIALS AND METHODS

Recruitment of the sample was carried out at the inpatient and outpatient services unit in Department of Psychiatry affiliated to tertiary health care multi-speciality teaching hospital in the state of Maharashtra.

A Cross Sectional, Observational, Non-interventional, Single time assessment, hospital-based study was carried out. Since the study is about identifying neurobiological association, for the sake of convenience to get modest sample size, we have used the Greenwoods formula[6] for identifying the sample size.

$$\widehat{Var}(\hat{S}(t)) = \hat{S}(t)^2 \sum_{t_i \le t} \frac{d_i}{n_i(n_i - d_i)}.$$

According to which we got a sample size of about 60, which we further divided into two subgroups of 30 patients each, first with predominant positive symptoms of schizophrenia (30), and other having patients with predominant negative symptoms (30). We have matched the 60 patients in relation to age and gender as we took 60 healthy controls for our study.

Patients of either gender, between 18 years to 60 years with family history of schizophrenia in first or second degree relative who are diagnosed cases of schizophrenia with predominant positive /or negative symptoms (diagnosed using International Classification of Disease-10 (ICD-10, Diagnostic and Clinical Research DCR criteria) [7] and who were willing to give written informed consent were included in study.

Subjects /patients with Subnormal intelligence, History of co-morbid diagnosed neurological disorder such as epilepsy or neurodegenerative disorders, Co-morbid substance abuse except nicotine use**,** History of head injury or having undergone recent neurosurgery, Suicidal/ homicidal / catatonic patients Female subjects /patients with pregnancy, Presence of Tardive dyskinesia / antipsychotic induced movement disorder(s) and whosoever refused to be a part of our study for any reason after due explanations for obtaining consent were excluded.

Assessment and Exclusive Evaluation of Minor Physical Anomalies-

Detailed history of patients attending psychiatric outpatient and inpatient department was taken and patients fulfilling criteria for International Classification of Diseases- 10 Axis I disorder of Schizophrenia[7] were recruited. Semi-structured proforma was used for collecting socio-demographic and clinical profile.

A total of 326 patients were initially screened to get through our inclusion and exclusion criteria as well as 30 patients of predominant positive symptoms and 30 patients of predominant negative symptoms to be successfully recruited for minor physical anomalies evaluation in our study. Out of the other 266 patients; some refused to participate in the study and some of them were not fulfilling the Inclusion and Exclusion criteria.

They were informed in detail regarding the study and written informed consent was taken in their local language (Marathi and/or Hindi). Socio-demographic data was collected on a semi-structured proforma modified from hospital inpatient standard clinical evaluation sheet. The respective schizophrenic patients from both groups were evaluated by PANSS[8] for the severity of positive and negative symptoms and each 30 subgroups of predominant positive and negative symptoms specifically by SAPS[9] and SANS[10] respectively. Further Clinical global severity assessment scale[11] was also used to measure their current status of improvement.

Patients were evaluated and clinically examined for the evaluation of minor physical anomaly assessment using the Waldrop and Halverson Scale[12] for Minor Congenital Anomaly. The Waldrop and Halverson Scale[12] for Minor Congenital Anomaly is 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 measurement of MPA has good test-retest reliability, inter-rater reliability and long-term stability. 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.

In this study we have used unweighted method to measure minor physical anomalies. Results were obtained and tabulated.

RESULTS

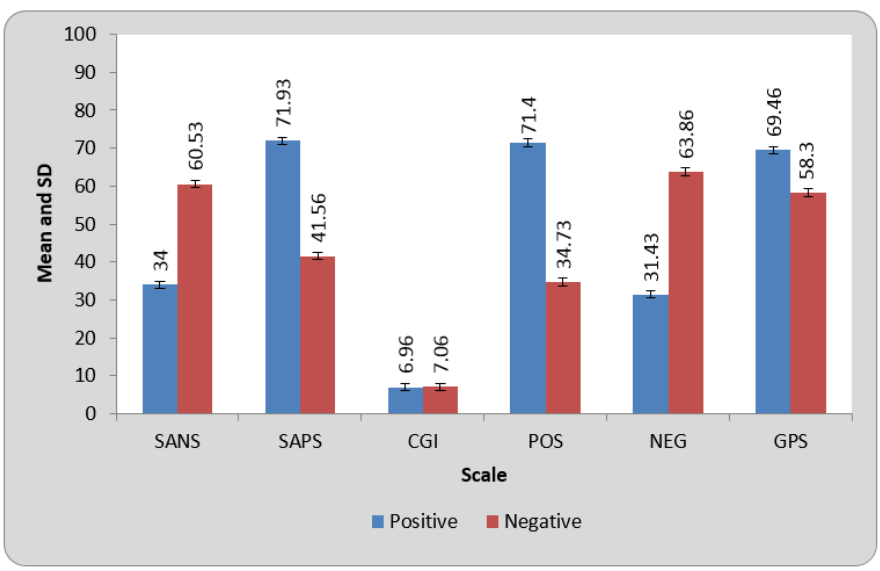
	Positive Subset	Negative Subset	t-value	p-value
SANS	34.0±10.11	60.53±14	8.41	0.0001, S
SAPS	71.93±9.49	41.56±12.28	10.71	0.0001, S
CGI	6.96±1.09	7.06±1.20	0.33	0.73, NS
PANSS				
POS	71.40±9.09	34.73±5.41	18.96	0.0001, S
NEG	31.43±5.56	63.86±6.98	19.83	0.0001, S
GPS	69.46±11.39	58.30±8.85	4.23	0.0001, S

Table 1. Comparative Distribution of Measures of Severity of Psychopathology between Positive and Negative Schizophrenic Patients

- POS- Positive Scale, NEG-Negative Scale, GPS-General Psychopathology Scale.

Table 1 shows the mean scorings of specific domains of positive and negative subsets of patients on SAPS, SANS, PANSS (subcategorized into the positive scale, negative scale and the general psychopathology scale) and the CGI scales.

Except for CGI (where values were comparable but non-significant (p value-0.73) in distribution), all the scores in specific domains were clearly specific and distinctly significant (p-0.0001) for SAPS, SANS and all subcategories on PANSS scales. This otherwise suggest that both groups are distinct, clearly different from each other and heterogenous as far as psychopathology and progression of illness is concerned (P value 0.001).



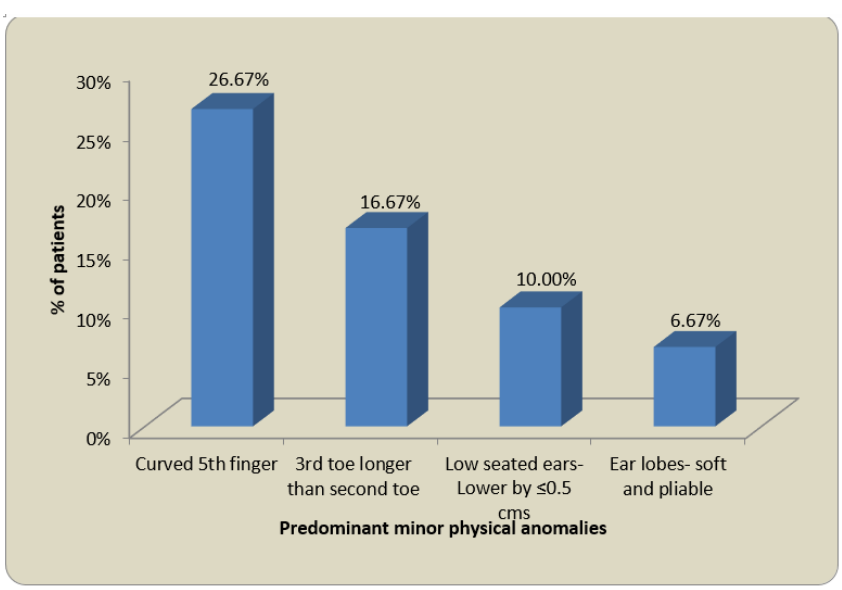
Graph 1. Graphical Distribution of Measures of Severity of Psychopathology Between Positive and Negative Subsets of Schizophrenic Patients

Minor Physical Anomalies	Positive	Negative	p-value
Head			
1. Fine electic hair	0(0%)	1(3.33%)	0.31, NS
2. 2 or more than 2 hair whorls	0(0%)	0(0%)	-
3. Circumference out of normal for age 3.1. >1 to <1.5 cms 3.2. >1.5 cms	 0(0%) 0(0%)	 0(0%) 0(0%)	-
Eyes			
4. Epicanthus – where upper and lower lids joined the nose, point of union is- 4.1 Partly Covered 4.2 Deeply Covered	 1(3.33%) 0(0%)	 2(6.67%) 0(0%)	0.55, NS
5. Hypertelorism – Approximate distance between the tear ducts 5.1 >1 to <1.5 cms 5.2 >1.5 cms	 2(6.67%) 0(0%)	 0(0%) 0(0%)	0.15, NS

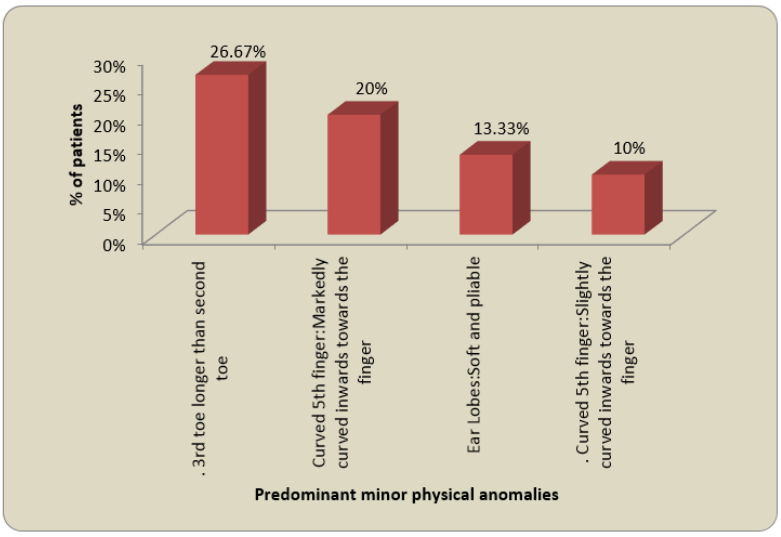
OR 5.3 6- 7 years=3.2 cms ≥ 3.3 cms 5.4 8-9 years = 3.3 cms ≥ 3.4 cms 5.5 10, 11, 12 years=3.4 cms ≥ 3.5 cms	0(0%) 0(0%) 0(0%)	0(0%) 0(0%) 0(0%)	
Ears	**Positive**	**Negative**	**p-value**
6. Low seated ears-point where ears joins the head, not in line with corner of eye and nose bridge 6.1 Lower by ≤0.5 cms 6.2 Lower by >0.5 cms	 4(13.3%) 0(0%)	 0(0%) 0(0%)	 0.002, S
7. Adherent ear lobes-lower end of ear extends- 7.1. Straight back towards rear of neck 7.2. Upward and back towards crown of hear	 2(6.67%) 0(0%)	 0(0%) 0(0%)	 0.15, NS
8. Malformed	0(0%)	1(3.33%)	0.31, NS
9. Asymmetric	4(13.3%)	0(0%)	0.002, S
10. Soft and pliable	4(13.33%)	4(13.33%)	-
Mouth			
11. High steeped palate-roof of mouth 11.1. Flat and narrow at top 11.2. Definitely steep	 0(0%) 0(0%)	 0(0%) 0(0%)	
12. Furrowed tongue (one with deep ridges)	0(0%)	1(3.33%)	0.31, NS
13. Smooth, rough spots on tongue	0(0%)	0(0%)	
Hands			
14. Curved 5th finger 14.1. Slightly curved inwards towards the 5th finger 14.2. Markedly curved inwards towards the 5th finger	 8(26.67%) 0(0%)	 3(10%) 6(20%)	 0.09, NS 0.009, S
15. Single transverse palmar crease	0(0%)	0(0%)	
Feet			
16. 3rd toe longer than second toe 16.1. Appears equal in length to 2nd toe	5(16.67%)	8(26.67%)	0.34, NS
17. Partial syndactyly of 2 middle rows	0(0%)	0(0%)	
18. Gap between 1st and 2nd toe approximately >1/4th of an inch	2(6.67%)	4(13.33%)	0.38, NS

Table 2. Comparison of Minor Physical Anomalies in Positive and Negative Subsets of Schizophrenic Patients

Table 2 depicts a long list of set of Minor Physical anomalies given by Waldrop and Halverson which were assessed in our study in 2 subsets of schizophrenic patients.



Graph 2.1: Predominant Minor Physical Anomalies in Positive Subset



Graph 2.2: Predominant Minor Physical Anomalies in Negative Subset

Variables	Positive Patients		Negative Patients	
	Correlation 'r'	p-value	Correlation 'r'	p-value
Age of onset	0.574	0.001, **S**	0.046	0.208, **NS**
Duration of Illness	0.352	0.056, **NS**	-0.235	0.210, **NS**
SANS Score	0.111	0.558, **NS**	0.101	0.594, **NS**
SAPS Score	0.575	0.001, **S**	-0.309	0.097, **NS**

Table 3. Correlation between Composite Score (Waldrop Score) of Minor Physical Anomalies for Positive and Negative Subsets of Patients

By using Pearson's correlation coefficient, we analysed the correlation of Waldrop score with set of significant clinical variables between both the subgroups of schizophrenia as noted in Table 3. We found a positive correlation of Waldrop score with age of onset (r=0.574) and total SAPS scores (r=0.575) in patients with predominant positive symptoms with very high level of significance (p value=0.001) while none of the factors could correlate significantly with Waldrop score as far as negative symptoms were concerned. Such correlation of Waldrop score with age of onset (years) reflect that patient who has one or other minor physical anomalies they are likely to have very early age of onset with more severe psychopathology compared to others.

DISCUSSION

Schizophrenia is widely held to be a neurodevelopmental disorder as proposed by Murray and Lewis (1987).[13] As the understanding of developmental brain abnormalities in schizophrenia is being strongly assumed to be originated during prenatal period which continues in childhood and adolescence. Although the characteristic symptoms of schizophrenia typically emerge in second or third decade of life, most of the time, positive symptoms precede the negative symptoms; many individuals commonly presented with some or other neurodevelopmental (MPA), abnormalities which can be measured and can have usefulness in predicting the later course in terms of severity and duration. Thus, the primary purpose of our study is to evaluate the presence of occult minor physical anomalies in both, positive as well as the negative subsets of schizophrenic patients, in both the subsets of schizophrenic patients. Consequently, an excess of MPAs does not appear to be specific to schizophrenia. This raises the question of whether the MPAs seen in schizophrenia differ from those seen in other disorders. Unfortunately, it is not possible to answer this adequately at present as most studies have presented data only in the form of total anomaly scores and the rates of individual anomalies are seldom described. This is probably because most studies to date have been based on relatively small samples and have lacked sufficient power to demonstrate statistically significant differences in individual anomalies.

Numerous studies to date have examined the relationship between MPAs and schizophrenia. These studies typically fall into one of the following two categories: those that compare the frequency of MPAs between schizophrenic or at-risk cases and healthy controls and those that explore the relationship between MPAs and other putative indices (morphological, cognitive, etc.) within a sample of schizophrenic individuals. Regarding studies that fall into the first category, there is general agreement that schizophrenic cases possess more MPAs than healthy controls.[14,15,16,] But in contrast study done by McNeil et al[17] (1992) failed to show a higher rate of minor physical anomalies in schizophrenia patients.

CONCLUSION

Increased MPA scores in schizophrenic patients in comparison to controls advocates that Minor Physical Anomalies may be considered as a useful

neuroendophenotypic marker for establishing an aetiopathogenesis in the schizophrenic disease process.

Strengths

1) Our study has a modest sample size of 60 which we believe is quite a sample when simultaneously we evaluated soft neurological signs, minor physical anomalies and psychopathology of schizophrenia mostly on clinical examination. Among such studies from India, Biswas et al has taken a sample size of only 35 from Chandigarh and Nizamie & Tikka[18] had a sample size of 40 which is comparatively less than ours.

Limitations

1) Our study is not devoid of limitations if we analyse it critically; for e.g. amongst several limitations, one of the major limitations which includes cross sectional study design in the hospital setting because only severe cases of schizophrenia comes to our hospital and one-time cross-sectional evaluation to establish fair degree of correlation can never be sufficient.
2) Since, the appearance of minor physical anomalies is a broader concept, which might probably take some time to evolve, may have fallen out of reach if the patient presents with an acute schizophrenic illness and complete & adequate co-operation has always remained a practical concern and therefore is subjected to examiners' bias.
3) There is a given possibility that a chronic schizophrenic patient at a given point of time may present with both positive as well as negative symptoms and the application of SAPS /SANS may not have been able to categorize the patient stringently into either of the subsets as evident from our study where almost as many as 23% of our negative symptom patients had their onset below 20 years of age. In other words, it may be possible that negative symptoms occur earlier to positive symptoms in small chunk of patients.
4) Finally, and unfortunately this endophenotypic study despite being having the proband(s) of positive history of psychosis in first degree relative; we failed to get their chromosomal linkage analyses which would have otherwise raised our understanding (if any) in providing the clues for further missing threads for aetiopathogenesis of enigmatic disorders like schizophrenia.

REFERENCES

[1] Weinberger DR, Wyatt RJ. Cerebral ventricular Size: a biological marker for subtyping chronic schizophrenia. In: Usdin E, Hanin I, eds. Biological markers in psychiatry and neurology. 1st edn. Oxford: Pregamon Press 1982:505-512.
[2] Watt NF. Longitudinal changes in the social behaviour of children hospitalized for schizophrenia as adults. J Nerv Mental Dis 1972;155:42-54.
[3] Bracha HS, Torrey EF, Bigelow LB, et al. Subtle signs of prenatal maldevelopment of the hand ectoderm in schizophrenia: a preliminary monozygotic twin study. Biological Psychiatry 1991;30(7):719-725.
[4] O'Callaghan E, Larkin C, Kinsella A, et al. Familial, obstetric and other clinical correlates of minor physical anomalies in schizophrenia. Am J Psychiatry 1991;148(4):479-483.
[5] Mednick SA, Machon RA, Huttunen MO, et al. Adult schizophrenia following prenatal exposure to an influenza epidemic. Arch Gen Psychiatry 1988;45(2):189-192.
[6] Greenwood M. The natural duration of cancer. Reports on Public Health and Medical Subjects. London: Her Majesty's Stationery Office 1926;33:1-26.
[7] WHO The ICD-10 classification of mental and behaviour disorder. Clinical description and diagnostic guidelines. Geneva, Washington DC: WHO 1992.
[8] Andreasen NC, Olsen S. Negative v positive schizophrenia. Definition and validation. Arch Gen Psychiatry 1982;39(7):789-794.
[9] Andreasen NC. The Scale for the assessment of positive symptoms (SAPS). Iowa City, IA: The University of Iowa 1984.
[10] Andreasen NC. The Scale for the assessment of negative symptoms (SANS). Iowa City, IA: The University of Iowa 1983.
[11] Guy W. Clinical Global Impressions (CGI) Scale. Modified From: Rush J. Psychiatric measures. APA Washington DC 2000.
[12] Ismail B, Cantor-Graae E, McNeil TF, et al. Minor physical anomalies in schizophrenic patients and their siblings. Am J Psychiatry 1998;155:1695-1702.
[13] Murray RM, Lewis SW. Is schizophrenia a neurodevelopmental disorder? Br Med J (Clin Res Ed) 1987;295(6600):681-682.
[14] Krouse JP, Kauffman JM. Minor physical anomalies in exceptional children: a review and critique of research. J Abnorm Child Psychol 1982;10(2):247-264.
[15] Smith DW. Recognizable patterns of human malformation. Philadelphia: WB Saunders 1970.
[16] Warkany J. Congenital malformations. Chicago, Year Book Medical 1971.
[17] O'Callaghan E, Buckley P, Madigan C, et al. The relationship of minor physical anomalies and other putative indices of developmental disturbance in schizophrenia to abnormalities of cerebral structure on magnetic resonance imaging. Biol Psychiatry 1995;38(8):516-524.
[18] Tikka SK, Nizamie SH, Das B, et al. Increased spontaneous gamma power and synchrony in schizophrenia patients having higher minor physical anomalies. Psychiatry Res 2013;207(3):164-172.