

## Prevalence and Characteristics of Cavum Septum Pellucidum in Schizophrenia: A 16 Slice Computed Tomography Study

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### ABSTRACT

**Objective:** Several significant midline abnormalities including cavum septum pellucidum (CSP) have been reported in schizophrenia. However, not all studies were able to replicate similar findings. Furthermore, very few of them were conducted with large samples. **Methods:** CSP was identified and graded with 16 slice computed tomography (CT) machine in 138 patients of schizophrenia and 64 controls. **Results:** We found 21.0% of patients in schizophrenia group had abnormal CSP compared to only 9.4% in control group ( $P = 0.047$ ). Grade III was most frequent type (19.6%) in schizophrenia group. **Conclusions:** Our study adds to the existing literature suggesting abnormal CSP may reflect neurodevelopmental process in schizophrenia. The strength of our study was larger sample size. Limitations were use of CT, male predominance in schizophrenia group, the inclusion of nonpsychiatric patients in control group.

**Key words:** Cavum septum pellucidum, characteristics, computed tomography, neuroimaging, prevalence, schizophrenia

### INTRODUCTION

Significant abnormalities in midline brain regions such as the corpus callosum, septum pellucidum, and cerebellar vermis have been found in patients with schizophrenia.<sup>[1-8]</sup> Among these cavum septum pellucidum (CSP) has been brain region of interest of researchers in recent times. CSP is a neurodevelopmental anomaly which is characterized by the presence of a thin plate of two laminae, which forms the medial wall of the lateral ventricles that fails to fuse forming a fluid filled

cavity.<sup>[9]</sup> Thus, enlarged CSP, if persists postnatally, has been proven to be a putative marker of disturbances in brain development contributing neuropsychiatric abnormalities.<sup>[3,9,10]</sup> Increased prevalence of CSP in patients with schizophrenia spectrum disorder (SSD) has, however, been inconsistently observed since it was originally described by Degreef *et al.*<sup>[11-13]</sup> The presence of CSP in patients with schizophrenia has

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been noted significantly more frequent than healthy controls (HCs) in female patients,<sup>[14]</sup> male patients,<sup>[15]</sup> chronic patients,<sup>[4,11,16,17]</sup> first episode patients,<sup>[4,12,18,19]</sup> as well as childhood onset schizophrenia.<sup>[5]</sup> However, several other studies including recent ones have not found a significant difference in frequency of CSP between patients with schizophrenia and HCs.<sup>[3,4,13,20-25]</sup> Hence, this study aimed to re-examine prevalence and qualitative nature of CSP in schizophrenia and to compare it with controls.

## METHODS

Ethical approval was obtained from Institutional Ethical Committee before collecting data.

### Subjects of schizophrenia group

This is a retrospective study which was undertaken at Central Institute of Psychiatry, Ranchi, India. Initially, all patients (aged between 18 and 60 years) diagnosed with schizophrenia, who had undergone computed tomography (CT) of the brain from January 2012 to December 2013 were included in this study. Diagnosis of schizophrenia was made according to Clinical Description and Diagnostic Guidelines, International Classification of Diseases-10<sup>th</sup> version by World Health Organization.<sup>[26]</sup> A total of 212 patients with schizophrenia had undergone CT of the brain in the said period. The method of chart review was adopted. Indications for neuroimaging were clinical suspicions of any organicity by treating psychiatrists or inadequate response to psychotropics. Any patient with a history of neurological illness, head injury with loss of consciousness, systemic illness with potential cognitive sequelae, or current substance abuse or history of substance dependence except nicotine and caffeine were excluded from this study. CT scans with abnormal findings other than enlarged CSP were excluded. Finally, a total of 138 patients were recruited for this study.

### Subjects of control group

Subjects of the control group were chosen from patients attending general outpatient department (OPD) of our institute. General OPD caters patients for minor physical ailments other than psychiatric illnesses. We selected all patients (aged between 18 and 60 years) from general OPD, who had undergone CT scan during the said period (January 2012–December 2013). A total of 87 patients had undergone CT of the brain during said period. The method of chart review was adopted. Common indications for neuroimaging are clinical suspicions of any neuropathology including vascular or space occupying lesions or degenerative changes, headache, dizziness. Any patient with a history of neurological illness, head injury with loss of consciousness, systemic illness with potential cognitive sequelae, or current substance abuse

or history of substance dependence except nicotine and caffeine were excluded from this study. None of the subjects in control group had any psychiatric illness. CT scans demonstrating vascular changes, degenerative changes, space-occupying lesions, or any other abnormal findings other than enlarged CSP were excluded from this study. Finally, 64 patients were included in this study as control group.

### Computed tomography acquisition

A Siemens 16 slice CT machine was used to obtain images for this study. As per imaging, protocol slices were obtained from base of skull through vertex with slice width 4.8 mm in the axial plane. Further, the images were reconstructed at thinner sections, up to 0.75 mm thickness in axial and coronal planes for detailed analysis. Length, width of cavity and width of septum were measured in the slice with largest dimension of CSP.

### CSP measurement

Two independent raters blinded to group membership of patients determined presence and grades of CSP. Two different criteria were used for CSP measurement. CSP was graded its length, width, and overall size on a scale of 0–4, as denoted 0 (absent), 1 (questionable), 2 (small), 3 (moderate), and 4 (severe).<sup>[10-13,16,27]</sup> Grade 0 was assigned if an intact septum pellucidum was clearly visible in all slices. Width of the CSP was graded as (a) unclear CSP, (b) distinct CSP, not wider than the thickness of the septum, (c) distinct CSP, wider than the thickness of the septum and occupying less than half of the ventricular space, or (d) CSP occupying at least half of the ventricular space. Furthermore, length of the CSP was graded as (a) CSP <1.5 mm, (b) CSP 1.5–6 mm, or (c) CSP ≥6 mm were taken into account to include in final grading scale. Finally, we assigned grades of CSP with the combination of CSP width and length. Further, they were divided as normal (Grades 0–1) and abnormal (Grades 2–4).<sup>[11]</sup> Each inter-rater disagreement was resolved through consensus.

### Statistical analysis

We used Chi-square test and Fisher exact test for categorical variables and Student's *t*-test for continuous variables.  $P < 0.05$  was considered statistically significant. Data were analyzed using Statistical Package for the Social Sciences version 20.0 for windows (Armonk, NY: IBM Corp).

## RESULTS

Our study sample consists of 138 patients of schizophrenia and 64 HCs. Although age was comparable between groups, sex differed significantly ( $P = 0.000$ ) with male predominance (81.2%) in schizophrenia

group [Table 1]. When frequencies for grades of CSP between groups were compared, significantly more ( $P = 0.002$ ) higher grades of CSP were observed in schizophrenia group. When CSP was divide as normal and abnormal according to used criteria, schizophrenia group had 21.0% of patients with abnormal CSP while only 9.4% of patients from HC group had abnormal CSP ( $P = 0.046$ ). No significant difference in frequency was observed between groups when only length of CSP was compared [Table 2].

## DISCUSSION

The literature to date has been inconsistent to precisely determine the prevalence of CSP in schizophrenia. Except two studies, to our knowledge, we had far more sample size than other studies.<sup>[25,28,29]</sup> This is the strength of our study. We found that between age-matched patients and controls, CSP was present in 23.2% of patients and 10.9% of HCs. Our study had 138 patients in the schizophrenia group. A recent meta-analysis has revealed the incidence of CSP ranged from 1.1% to 89.7% in healthy volunteers,<sup>[27,29]</sup> and from 10.0% to 89.5% in patients with SSDs.<sup>[28-30]</sup> The findings were irrespective of CSP dimensions. The finding was similar for both chronic<sup>[11,14,20,27,31]</sup>

and first episode patients.<sup>[11,16]</sup> Noteworthy is that few other studies did not find significant differences in the prevalence of CSP between SSD patients and healthy participants.<sup>[3,4,13,18,21,23,25,29,30]</sup> Differences in methodology across studies might be responsible for this wide discrepancy in the reported prevalence and size of CSP. All of the studies discussed above did not use homogenous sample. In addition, the criterion used for measurement of CSP and its prevalence differed across studies.<sup>[28]</sup> Except one, none of the magnetic resonance imaging (MRI) studies had sex-matched control group for comparison.<sup>[29]</sup> With the evidence that male patients may present a higher occurrence of any or large CSP than male healthy participants,<sup>[3,23,31,32]</sup> the reported prevalence rate in our study for CSP thus might be confounded by sex. Thus, male predominance in schizophrenia group might contribute to higher prevalence of CSP. In contrast to gender-related effect, the nature of age-related effect on CSP prevalence is not straight one. While none of the MRI studies to date showed significant correlations between age and CSP measures, researches have shown age-related volumetric differences in brain structures in the vicinity of CSP.<sup>[28,33,34]</sup> Thus, prevalence rates reported in our study is free of any age-related confounding effect. Regarding CSP dimensions, we found CSP of higher grades were more prevalent than CSP of lower grades in schizophrenia group. Thus, abnormal CSP was more prevalent than normal CSP in schizophrenia group. This finding is in parallel with other studies and reflects the notion that it is abnormal or enlarged CSP but not normal CSP, which might reflect pathology in the limbic system, corpus callosum or hippocampus, all of which are implicated in schizophrenia.<sup>[31,32]</sup> This is consistent with neurodevelopmental theory of schizophrenia which suggest abnormal trajectory of brain development as a key pathological process of this illness.<sup>[35]</sup> A recent meta-analysis supports this evidence and found no significant differences in the prevalence of CSP of any size between SSD patients and healthy participants while incidence of a large CSP was higher in SSD patients than in healthy volunteers.<sup>[28]</sup> However, some studies which used more quantitative and reliable method by counting the number of slices in which the CSP cavity clearly appears, especially on coronal MRI views, have found conflicting results. This might only be explained by heterogeneity of samples and difference in criteria used to define abnormal or enlarged CSP.<sup>[28]</sup>

## Limitations

There are certain limitations in our study. We used CT instead of MRI, which have more sensitivity and thus might yield more accurate measures of CSP. We did not have gender matched control group which might confound prevalence rate of CSP between groups.

**Table 1: Comparison of age and sex between groups**

	Patients (n=138) (%)	Controls (n=64) (%)	$\chi^2/t$	df	P
Age (years) mean±SD	33.41±9.57	33.97±12.42	-0.348	100	0.728
Sex					
Male	112 (81.2)	34 (53.1)	17.150*	1	0.000**
Female	26 (18.8)	30 (46.9)			

\* Level of significance accepted at  $P=0.05$ ; \*\* Level of significance accepted at  $P=0.01$ ; SD – Standard deviation

**Table 2: Comparison of cavum septum pellucidum between groups according to criteria**

CSP grades	Patients, n=138 (100%)	Controls, n=64 (100%)	$\chi^2$	df	P
Grade 0					
Absent	106 (76.8)	57 (89.1)	14.126	4	0.002**
Grade 1					
Questionable	3 (2.2)	1 (1.6)			
Grade 2					
Small	0 (0.0)	3 (4.7)			
Grade 3					
Moderate	27 (19.6)	3 (4.7)			
Grade 4					
Large	2 (1.4)	0 (0.0)			
Normal (Grade 0 + Grade 1)	109 (79.0)	58 (90.6)	4.135	1	0.047*
Abnormal (Grade 2 + Grade 3 + Grade 4)	29 (21.0)	6 (9.4)			

\* Level of significance accepted at  $P=0.05$ ; \*\* Level of significance accepted at  $P=0.01$ ; CSP – Cavum septum pellucidum

The control group of our study did not comprise with healthy volunteers. Finally, retrospective design limits adequacy of our data.

## CONCLUSIONS

Our study found CSP in patients of schizophrenia within reported range in existing literature. Although we found abnormal CSP were significantly more commonly found in patients with schizophrenia and thus adding to the existing literature on neurodevelopmental disease process, this should be interpreted with caution due to limitations of study we discussed. Further studies will likely benefit from use of more quantitative methods by MRI, the inclusion of gender matched HCs.

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## Conflicts of interest

There are no conflicts of interest.

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