



## Review Article

## Emerging role of MRI to assess the Volume of Pineal Glands in Schizophrenia and Mood Disorders: Literature Review

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## ARTICLE INFO

## Key Words:

Bipolar Disease, Schizophrenia, Unipolar Depression, Pineal Gland Volume

## How to Cite:

 Raza, M. A., Parveen, R., Sultan, H., Altuf, L., Sana, A., & Zafar, F. S. (2023). A. Emerging role of MRI to assess the Volume of Pineal Glands in Schizophrenia and Mood Disorders: Literature Review: Emerging Role of MRI. *Pakistan Journal of Health Sciences*, 4(09). <https://doi.org/10.54393/pjhs.v4i09.1027>

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 Received Date: 9<sup>th</sup> September, 2023

 Acceptance Date: 29<sup>th</sup> September, 2023

 Published Date: 30<sup>th</sup> September, 2023

## ABSTRACT

Most patients with manic depression and diseases have issues with their circadian rhythms and sleep. Melatonin, which is vital for circadian rhythm and sleep, is secreted by pineal gland. This study evaluated and compared the volume of pineal gland in individuals with psychotic symptoms and manic depression. The aim of study is to find out volume of Pineal glands in Schizophrenic Patients. The data included in this literature review were found using several search engines. Using magnetic resonance imaging, the total mean pineal volume compared with the total pineal gland volume of all patients. In this research's literature evaluation, only 26 articles were used for extraction of data related to topic statement. The current study looked role of MRI to assess volume of pineal gland in in Schizophrenic patients. Patients with manic depression had considerably lower mean volume of pineal gland than the other groups. It is concluded that although more research is needed to fully understand the aspects of medications and more mediating agents on the volume of pineal gland. This difference is not present in patients with manic depression. Pineal gland abnormalities in schizophrenia patients may contribute to the disease's etiology.

## INTRODUCTION

Disruptions of the circadian rhythm in patients are commonly linked to manic depression [1]. These anomalies are signs of recurrence that are brought on by persistent symptoms and resistance to therapy [2]. They put people at risk for developing psychological problems. Pineal gland metabolism and mental disorder have long been thought to be related [3, 4]. The size of pineal gland is a small, pinecone-shaped part that controls mental & behavioral changes and sleep by regularly secreting the hormone melatonin [5]. The sleep-wake cycle is created by a circadian pacemaker, it is released in accordance with the 24-hour cycle. The release of melatonin is timed to peak

levels occurring at night in 24-hours the 24-hours by an oscillator in endogenous circadian rhythms [6]. Patients with manic depression and bipolar disorders have been demonstrated to have altered melatonin production, altered diurnal or nocturnal peaks, and aberrant pineal function [7, 8]. It is essential to recognize irregularities in the circadian rhythm in order to better comprehend probable psychiatric illness prevention, causes, processes, sustaining factors, and therapies. There isn't many researches that we are aware of that look at the connection between volume of pineal glands and mental disorders. This research used radiological methods including (MRI)

and cerebral (CT), the results of which are unclear (MRI) [9, 10] found no difference in total volume of pineal gland b/w man depression. Contrarily, male schizophrenia patients' pineal volumes were shown to be lowered by Bersani *et al.*, found that patients with sleep disorder had lower volume of pineal glands rather than healthy peoples [11]. In the current work, we seek to quantify and contrast the volume of pineal glands in individuals with schizophrenia & manic disorders.

## METHODS

Data from several search engines were retrieved for this systematic review. Data for this literature study were gathered from PubMed, Medline, Science Direct, NCBI, Medscape, and Google Scholar. Bipolar disorder, schizophrenia, unipolar depression, and pineal gland volume were utilized as search terms for publications. Only those papers that show that individuals with schizophrenia have a considerably lower pineal gland volume than healthy persons were included after conducting unbiased database searches. Research was evaluated for both its quality and its usefulness. Data extraction from whole journal articles was done.

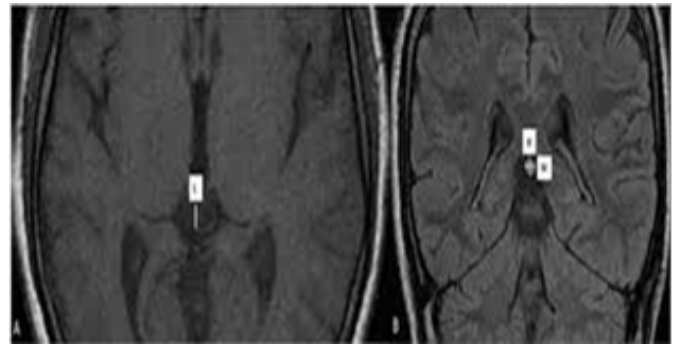
### MRI procedure

The identical 1.5 Tesla device was used for all MRI examinations. Axial FLAIR, axial T2\*-FLASH, axial triple echo T2-TSE, and genuine FISP made up the experimental methods. Using the proper measuring software on previously captured T1 weighted MRI images, one dimensional measures of epiphysis cerebri were impulsive gathered for individual person. An assessment were representing by experience MR-specialist with the patients' identities and other protocol-related information kept secret. The quadrigeminal cisterna, the posterior third ventricle, and the superior colliculus were used as indicators for deciding which axial incision to make.

## RESULTS

A literature review of more than 26 articles was included in this review, it is found that the Age and gender distributions were similar across the patient and experimental group ( $p > 0.05$ ). Sum of pineal gland varied between controls ( $99.74 \pm 12.04 \text{ mm}^3$ ), UD patients ( $95.19 \pm 11.61 \text{ mm}^3$ ), BD patients ( $93.62 \pm 11.00 \text{ mm}^3$ ), and schizophrenia patients ( $83.5 \pm 10.11 \text{ mm}^3$ ). The only statistically significant difference between schizophrenia patients and controls was the mean pineal gland volume ( $p = 0.001$ ). Furthermore, when patient groups were examined, those with schizophrenia had considerably lower volume of pineal gland than those with depression and bipolar disorder. Although there was a polarity in epiphysis cerebri allying the manic depression and UD groups, this difference was not statistically significant ( $p = 0.722$ ). In schizophrenia

patients, there was no statistically significant correlation between volume of pineal gland and age at the onset illness ( $r = -0.244$ ,  $p = 0.404$ ), disease spell ( $-0.335$ ,  $p = 0.242$ ), or treatment duration ( $-0.238$ ,  $p = 0.412$ ). Additionally, mean average epiphysis cerebri volumes of female in the schizophrenia group were lower than those of men, although this difference was not analytical significant ( $78.9 \pm 7.5$  vs.  $86.5 \pm 10.5 \text{ mm}^3$ ,  $p = 0.129$ ).



**Figure 1:** (A) MRI images with length of the pineal gland on axial T1W- image, (B) The height and width of the pineal gland on FLAIR

## DISCUSSION

Majority startling finding of research was how much smaller pineal glands were in those with schizophrenia compared to people with mood disorders. It implies that the melatonergic system of the pineal gland and an irregular circadian rhythm may have a role in mood disorders and schizophrenia [12]. There were no volumetric differences in the pineal gland between schizophrenia patients and normal individuals, according to Sun *et al.*, However, none of the study's possible confounding variables—drugs, the age at which the sickness first appeared, how long people took their medications, or pineal cysts—were taken into account [13]. It is found reduced pineal volume in male schizophrenia patients, were similar to those of our study. Although the schizophrenia group in our research had longer mean illness and treatment durations than the other groups [14]. In the research, individuals with schizophrenia had shorter mean durations of illness and treatment than those with schizophrenia in our study. But they arrived at conclusions that agreed with those of our investigation, which revealed that individuals with schizophrenia had small volume of pineal glands. This shows that the duration of the sickness or treatment has little effect on pineal volume. We thus reasoned that the decrease in volume of pineal glands would be caused by detain intellectual disorders in affected peoples [15]. Early developmental delays may occur in the pineal gland, and neurodegeneration may cause molecular damage and subsequent pineal gland shrinkage. Degenerative processes are clearly calcific processes. According to the results of CT studies, pineal calcification

is highly linked with the early onset of schizophrenia and prefrontal cortical atrophy [16]. Thus, we speculate that coagulation may be the cause loss of neurons. This physical change may also be caused by a hypofunctional pineal gland or by other hormonal, genetic, or other factors. The absence of a perceptible polarity of epiphysis cerebri was the second most remarkable result of our investigation. We believe that research is most common to examine the connection in bipolar disorders. The results of Sarrazin et al., research, which compared the extent of epiphysis cerebri volumetric size of the pineal gland in different patients were in line. They came to the conclusion that rather than the structure of the gland, pineal dysfunction may be connected to the gland's functioning characteristics [17]. It is unknown there are no differences in volume of pineal gland in behavioral disorders. One theory is that morphology of pineal gland has no impact on level of melatonin. Additionally, modifications in the melatonin production pathway have just lately been related to mental conditions as depression and bipolar disorder [18, 19]. One vital enzyme in the production of melatonin is the acetyl serotonin O-methyltransferase (ASMT). The gland's decreased functional capacity could be related to this enzymatic process. Psychotropic drugs may influence pineal gland shape and melatonin release in mental diseases through conceivable but unidentified biochemical routes. Every single one of our patients was on medicine, which included antipsychotics, valproate, lithium, and antidepressants. The melatonin secretory pattern was unaffected by long-term antipsychotic drug usage [20]. Olanzapine therapy did not substantially change the melatonin production in schizophrenic patients [21]. Lithium had no effect on melatonin's total production or its start in low light [22]. Noted that selective serotonin high the sleep hormone, albeit the process remained imprecise. The production of nocturnal melatonin is decreased by benzodiazepine [23, 24]. Antidepressants, lithium, and valproate, which modify melatonin levels, may have a complex effect on pineal gland volumes in UD and BD patients. Previous studies imply a relationship between blood levels of melatonin and pineal gland volume, which may be assessed by MRI [25, 26]. Melatonin concentrations were not assessed during our experiment. It is unknown if therapy along different medicines changes the sleep hormone level consequently cerebri size because we were unable to search the studies detailing the attain of psychiatric medicines on epiphysis cerebri size. This research also found that there is no evidence to gives the idea that psychiatric drugs could change volume of pineal gland or the length of therapy. Therefore, additional information is necessary to understand how various medications influence the pineal gland. There are some

substantial gaps in our study. The average size was at first somewhat slight. A second investigator who had been blindfolded did not do manually. Different patient groups may have different levels of pineal calcification, which might reject review. In this study calcifications cannot be accurately assessed by MRI. Sleeping hormone level weren't checked. It may helpful to track changes in pineal hormone as the disorders get worse.

## CONCLUSIONS

It is concluded that although more research is needed to fully understand the medication effects and related factors on volume of pineal gland, schizophrenic patients have decrease volume of pineal glands rather than healthy peoples. This difference is not present in effected persons with manic diseases. Pineal gland abnormalities in schizophrenia patients may contribute to the disease's etiology.

## Authors Contribution

Conceptualization: MAR

Methodology: RP

Format Analysis: HS, LA, MAR

Writing-review and editing: AS, FSZ

All authors have read and agreed to the published version of the manuscript

## Conflicts of Interest

The authors declare no conflict of interest.

## Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

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