# To evaluate serum cortisol levels in patients with alcohol withdrawal delirium v/s patients with delirium due to any other disorder

**Ishrat Sibia, Angad H. Singh, Rahul Joshi, Deepak Khanduja, Manish Bathla**

*Department of Psychiatry, Maharishi Markandeshwar Institute of Medical Sciences and Research, Ambala, Haryana, India*

## ABSTRACT

**Background:** Delirium is an acute confusional state characterized by changes in the mental status, level of consciousness, impaired cognition, and inattention. It can develop within hours or days. Cortisol release from the hypothalamic–pituitary–adrenal axis (HPA) is vital for the host survival in stress. Biomarkers are used as an indicator of pathogenic processes or to assess the responses to a therapeutic intervention. To improve delirium recognition and care, investigators have identified possible biomarkers that may help in diagnosing individuals with delirium, assessing the severity of delirium. Cortisol has been suggested as biomarker for the diagnosis of delirium. **Aims and Objectives:** To evaluate and compare levels of serum cortisol in patients with alcohol withdrawal delirium with delirium due to other disorders. **Materials and Methods:** It was a cross-sectional prospective observational study. A total of 30 patients in Group A and 32 in Group B were included. The participants were evaluated based on delirium rating scale (DRS). **Results:** It was seen that in alcohol withdrawal delirium group, there was significant positive correlation between DRS score and serum cortisol level, i.e., with increase in DRS score, there was increase in serum cortisol levels and vice versa. **Conclusion:** Serum cortisol levels are associated and directly correlate with the occurrence and severity of delirium. Further studies are needed to elucidate the implications of this association for diagnosis and treatment.

**Keywords:** Biomarkers, delirium, DRS, ICU, serum cortisol

## Introduction

Delirium is an acute confusional state characterized by changes in the mental status, level of consciousness, impaired cognition, and inattention.[1] It can develop within hours or days. Rapid fluctuations between hypoactive and hyperactive states with periods of intermittent lucidity are seen in some patients.[1] It may be mostly identified in patients with sleep/wake cycle disturbances, emotional lability, hallucinations, or delusions.[2] Emergency reports that about 10–15% of the older adults present with delirium.[3]

It is usually caused by multiple etiologies and the exact pathophysiology of delirium remains poorly understood.[4,5] Cortisol release from the hypothalamic–pituitary–adrenal axis (HPA) is vital for the host survival in stress.[6] In sepsis, high cortisol release could result from stress as well as from HPA dysfunction and following a reduced metabolism of this hormone at the organs.[7-9] An excessive release or chronic exposure to high cortisol levels could be harmful for the host brain, especially at the hippocampus and the frontal cortex where corticoid receptors are highly concentrated.

Biomarkers are used as an indicator of pathogenic processes or to assess the responses to a therapeutic intervention. To improve delirium recognition and care, investigators have identified possible biomarkers that may help in diagnosing individuals with

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delirium, assessing the severity of delirium, defining end points for the resolution of delirium, developing new therapies, and monitoring response to treatment.

Cortisol has been suggested as biomarker for the diagnosis of delirium.[10] High cortisol release associated with delirium has been reported in stroke[11] in postcardiac surgery,[12] in the elderly patients with hip fracture,[13] in psychological depression, and in Cushing's syndrome.[14]

About 80% of ICU patients develop delirium, and many patients who do not have alcohol use disorders develop the disorder as well.

Cortisol is also higher in patients who are at increased risk of dying from severe infections. The aim of this study is to see if cortisol levels are higher in patients with alcohol withdrawal delirium as compared to those who have delirium due to cause other than alcohol withdrawal.

## Aims and Objectives

To evaluate and compare levels of serum cortisol in patients with alcohol withdrawal delirium with delirium due to other disorders.

## Materials and Methods

It was a cross-sectional prospective observational study. Patients admitted in ICU in our institute between September and December 2021 in the age group of 18–70 years with delirium as defined by ICD-10/DSM-5. A total of 30 patients in Group A and 32 in Group B were included. Written and informed consent was taken from their caretakers, and institutional ethical committee clearance was taken before data collection. The participants were evaluated based on DRS. They were assessed for inclusion and exclusion criteria and were assigned respective groups A and B.

In Group A, we included patients admitted in ICU with alcohol withdrawal delirium. In Group B, patients admitted in ICU with delirium due to any cause other than alcohol withdrawal delirium were included. Patients having previous history of mental illness, having language, vision, hearing impairment, and who did not have the basic level of education were excluded from both the groups. Data was entered into Microsoft Excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Independent t-test was used as test of significance to identify the mean difference between two quantitative variables and qualitative variables, respectively. Graphical representation of data: MS Excel and MS Word were used to obtain various types of graphs such as bar diagram.

P-value of <0.05 was considered as statistically significant after assuming all the rules of statistical tests. Statistical software: MS

Excel**,** SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

## Results

A total of 30 patients in Group A and 32 in Group B were included. Table 1 shows patient's age distribution between both the groups. In alcohol withdrawal delirium group, 13.33% were in 19–30 years, 26.67% were in 31–40 years, 33.33% were in 41–50 years, 10% were in 51–60 years, and 16.67% were in 61–70 years. In delirium due to cause other than alcohol, 18.75% were in 19–30 years, 9.38% were in 31–40 years, 18.75% were in 41–50 years, 21.88% were in 51–60 years, and 31.25% were in 61–70 years. There was no significant difference in patient's age distribution between two groups. Table 2 shows that in alcohol

### Table 1: Patient's age distribution between two groups

|  | Diagnosis | | | |
|  | Alcohol withdrawal delirium | | Delirium due to cause other than alcohol | |
|  | Count | Column *n* % | Count | Column *n* % |
|---|---|---|---|---|
| Patient's age |  |  |  |  |
| 19-30 Years | 4 | 13.33% | 6 | 18.75% |
| 31-40 Years | 8 | 26.67% | 3 | 9.38% |
| 41-50 Years | 10 | 33.33% | 6 | 18.75% |
| 51-60 Years | 3 | 10.00% | 7 | 21.88% |
| 61-70 Years | 5 | 16.67% | 10 | 31.25% |

### Table 2: Gender distribution between two groups

|  | Diagnosis | | | |
|  | Alcohol withdrawal delirium | | Delirium due to cause other than alcohol | |
|  | Count | Column *n* % | Count | Column *n* % |
|---|---|---|---|---|
| Gender |  |  |  |  |
| Male | 29 | 96.67% | 4 | 12.50% |
| Female | 1 | 3.33% | 28 | 87.50% |

$\chi^2$=44.059, df=1, $P$=<0.001*

### Table 3: Co-morbidities distribution between two groups

|  | Diagnosis | | | |
|  | Alcohol withdrawal delirium | | Delirium due to cause other than alcohol | |
|  | Count | Column *n* % | Count | Column *n* % |
|---|---|---|---|---|
| Co-morbidities |  |  |  |  |
| Present | 18 | 60.00% | 19 | 59.38% |
| Absent | 12 | 40.00% | 13 | 40.63% |

$\chi^2$=0.003, df=1, $P$=0.96

### Table 4: Mean DRS-98 score comparison between two groups

|  | Diagnosis | | | | *P* |
|  | Alcohol withdrawal delirium | | Delirium due to cause other than alcohol | | |
|  | Mean | SD | Mean | SD | |
|---|---|---|---|---|---|
| DRS-98 SCORE | 19 | 3.03 | 17.09 | 1.61 | 0.003* |

### Table 5: Mean serum cortisol level comparison between two groups

| | Diagnosis | | | | P |
|---|---|---|---|---|---|
| | Alcohol withdrawal delirium | | Delirium due to cause other than alcohol | | |
| | Mean | SD | Mean | SD | |
| Serum cortisol level | 571.27 | 476.97 | 429.66 | 376.01 | 0.198 |

### Table 6: Correlation between DRS score and serum cortisol level in alcohol withdrawal delirium group

| | DRS-98 score | Serum cortisol level |
|---|---|---|
| DRS-98 score | | |
| Pearson's correlation | 1 | 0.373* |
| P | | 0.043 |
| n | 30 | 30 |

Alcohol withdrawal delirium

### Table 7: Correlation between DRS score and serum cortisol level in Delirium due to cause other than alcohol

| | DRS-98 score | Serum cortisol level |
|---|---|---|
| DRS-98 score | | |
| Pearson's correlation | 1 | -0.041 |
| P | | 0.824 |
| n | 32 | 32 |

a. Diagnosis=Delirium due to cause other than alcohol

withdrawal delirium group, 96.67% were male and 3.33% were female. In delirium due to cause other than alcohol, 12.5% were male and 87.5% were female. There was a significant difference in gender distribution between two groups.rence in gender distribution between two groups. In Table 3 we can see that 60% had comorbidities and 59.38% had comorbidities in delirium due to cause other than alcohol group.

In Table 4 Mean DRS-98 SCORE in alcohol withdrawal delirium group was 19 ± 3.03 and in delirium due to cause other than alcohol group was 17.09 ± 1.61. Table 5 concluded that there was no significant difference in mean serum cortisol level comparison between two groups. In Tables 6 and 7 we can se that In alcohol withdrawal delirium group, there was significant positive correlation between DRS score and serum cortisol level, i.e., with increase in DRS score, there was increase in serum cortisol levels and vice versa.

## Discussion

Biomarkers accurately predicting delirium before its development would be crucial in terms of providing pathways for therapeutic drugs. Cortisol is a hypothalamic–pituitary–adrenal axis hormone and has already been investigated in surgical patients mostly at perioperative phases. Raised perioperative plasma cortisol concentrations are associated with delirium after coronary artery bypass graft surgery. This may be an important pathophysiological consideration in the increased risk of postoperative delirium seen in patients.

In the current study in alcohol withdrawal delirium group, maximum patients were in the age group of 41–50 years while in the other group maximum were in the age group of 51–60 years. There was no significant difference in patient's age distribution between two groups.

In alcohol withdrawal delirium group, maximum patients were male in delirium due to cause other than alcohol; mostly the patients were female. There was a significant difference in gender distribution between two groups which might be due to high alcohol consumption among males as compared to females in the population our hospital caters to.

In the current study, mean DRS-98 score in alcohol withdrawal delirium group was 19 ± 3.03 and in delirium due to cause other than alcohol group was 17.09 ± 1.61. There was a significant difference in mean DRS-98 score comparison between two groups. A score of >18 is indicative of delirium. In alcohol withdrawal delirium group, there was significant positive correlation between DRS score and serum cortisol level, i.e., with increase in DRS score, there was increase in serum cortisol levels and vice versa. In a study done by Colkesen[15] *et al.*, it was seen that elevated serum cortisol levels were associated with increased risk of delirium. It was seen that the levels of cortisol had a direct co-relation with severity of delirium. The results were in lines with our study.

A study found that elevated serum cortisol level was associated with an increased incidence of postoperative delirium in critically ill patients after noncardiac surgery.[16] There have been studies that found a relation between serum cortisol levels and postoperative cardiac surgery,[17] but there are very few studies to co-relate relationship between alcohol withdrawal delirium and serum cortisol levels. It has been suggested that stress and high circulating glucocorticoid levels can produce deterioration in neuropsychological function.[18]

Thus, further studies are needed to elucidate the mechanisms by which circulating cortisol levels affect delirium.

In delirium due to cause other than alcohol group, there was no significant correlation between DRS score and serum cortisol level. Negative correlation was observed between DRS score and serum cortisol levels.

There were some limitations in our study. The sample size was small, and only a single cortisol level was measured early inpatient's hospital course. We have not found another similar study in literature that would enable us to correlate our results. Baseline cortisol levels were not measured, which might have added to the interpretation of the relationship between cortisol level and the occurrence of delirium. It is possible that the change in cortisol from baseline rather than the height of a single

measurement would be a better reflection of the risk of delirium. As there were few patients in this study, we need a bigger sample size to identify the best cutoff level and correlate the relationship between delirium and serum cortisol levels.

## Conclusion

Serum cortisol levels are associated and directly correlate with the occurrence and severity of delirium. Further studies are needed to elucidate the implications of this association for diagnosis and treatment.

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### Conflicts of interest

There are no conflicts of interest.

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