Section: General Medicine

Original Research Article

HYPOMAGNESEMIA AND SEVERITY OF ALCOHOL WITHDRAWAL SYNDROME: A HOSPITAL-BASED CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Alcohol Withdrawal Syndrome (AWS) is a frequent complication among individuals with alcohol use disorder and is associated with significant morbidity and mortality. Chronic alcohol consumption commonly leads to hypomagnesemia due to poor nutritional intake, gastrointestinal losses, and renal magnesium wasting. Magnesium deficiency may aggravate neuroexcitability, seizures, autonomic instability, and cardiac arrhythmias during withdrawal.[1,2] However, data correlating serum magnesium levels with severity of AWS remain limited, particularly in the Indian population. The Objective is to evaluate serum magnesium levels in patients with Alcohol Withdrawal Syndrome and to determine their association with withdrawal severity assessed using the Clinical Institute Withdrawal Assessment for Alcohol-Revised (CIWA-Ar) score. **Materials and Methods:** This hospital-based cross-sectional study was conducted among 100 male patients admitted with Alcohol Withdrawal Syndrome at Government General Hospital, Guntur. Patients fulfilling DSM-5 diagnostic criteria for AWS and abstinent from alcohol for at least 6 hours were included. Serum magnesium and other biochemical parameters were measured at admission. Withdrawal severity was assessed using the CIWA-Ar scale. Statistical analysis included one-way ANOVA, Student's t-test, and Pearson correlation analysis. **Results:** The mean serum magnesium level of the study population was 1.12 ± 0.59 mg/dL. Severe withdrawal symptoms (CIWA-Ar >20) were observed in 58% of patients. Serum magnesium levels demonstrated a significant decline with increasing withdrawal severity, with mean levels of 1.95 ± 0.16 mg/dL in patients with CIWA-Ar <10 compared to 0.71 ± 0.35 mg/dL in patients with CIWA-Ar >20 ($p<0.001$). A strong negative correlation was observed between CIWA-Ar score and serum magnesium levels ($r = -0.808$, $p<0.001$). Serum potassium levels also showed significant negative correlation with withdrawal severity ($r = -0.693$, $p<0.001$). **Conclusion:** Hypomagnesemia is highly prevalent among patients with Alcohol Withdrawal Syndrome and is strongly associated with increased withdrawal severity. Routine assessment of serum magnesium may help identify high-risk patients and facilitate early corrective management in AWS.

INTRODUCTION

Alcohol Withdrawal Syndrome (AWS) is a common and potentially life-threatening complication observed in individuals with alcohol use disorder following abrupt cessation or reduction of prolonged alcohol consumption. Clinical manifestations range from mild tremors, anxiety, and autonomic hyperactivity to severe complications such as seizures, hallucinosis, and delirium tremens.[1] Chronic alcohol consumption is also associated with multiple metabolic and electrolyte disturbances, among which hypomagnesemia is one of the most frequent and clinically significant abnormalities.[2,3] Magnesium is an essential intracellular cation that acts as a cofactor in more than 300 enzymatic reactions and plays a critical role in neuromuscular transmission, cardiac electrophysiology, membrane stabilization, and regulation of neuronal excitability.[4] Magnesium additionally functions as a physiological antagonist of the N-methyl-D-aspartate (NMDA) receptor, thereby limiting glutamate-mediated excitotoxicity. Reduced magnesium levels lower the threshold for neuronal excitation and may contribute to increased severity

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of alcohol withdrawal manifestations, including seizures and autonomic instability.[4,5]

Individuals with chronic alcohol use disorder are particularly predisposed to magnesium deficiency due to inadequate nutritional intake, gastrointestinal losses, vomiting, diarrhea, renal magnesium wasting, and alcohol-induced tubular dysfunction.[5,6] Previous studies have demonstrated that hypomagnesemia is highly prevalent among patients admitted with alcohol withdrawal syndrome and is frequently associated with concurrent electrolyte abnormalities such as hypokalemia and hyponatremia.[7] Observational studies have further suggested that lower serum magnesium levels may correlate with adverse clinical outcomes in patients undergoing alcohol withdrawal.[8]

Several investigators have evaluated the therapeutic role of magnesium supplementation in AWS; however, existing evidence remains inconclusive. While some studies have reported improvement in withdrawal symptoms and faster clinical recovery with magnesium supplementation, others have failed to demonstrate significant clinical benefit.[9-11] Furthermore, a systematic review concluded that the available evidence is insufficient to support routine magnesium supplementation for alcohol withdrawal syndrome.[12] Despite these inconsistencies, assessment of serum magnesium remains clinically relevant because untreated hypomagnesemia may aggravate seizures, cardiac arrhythmias, refractory hypokalemia, and metabolic instability during withdrawal.[5]

Although hypomagnesemia in alcohol use disorder has been extensively investigated in Western populations, data evaluating its association with alcohol withdrawal severity in Indian patients remain limited. A study from India reported a significant association between lower serum magnesium levels and increased severity of alcohol withdrawal manifestations, highlighting the need for further evidence from Indian settings.[13] Therefore, the present study was undertaken to evaluate serum magnesium levels in patients with Alcohol Withdrawal Syndrome and to determine their relationship with withdrawal severity using the Clinical Institute Withdrawal Assessment for Alcohol-Revised (CIWA-Ar) score.

Objectives

- To measure serum magnesium levels in chronic alcoholic patients presenting with Alcohol Withdrawal Syndrome after abstinence from alcohol for a minimum duration of 6 hours.
- To determine the relationship between serum magnesium levels and the severity of alcohol withdrawal symptoms assessed using the Clinical Institute Withdrawal Assessment for Alcohol-Revised (CIWA-Ar) score.

MATERIALS AND METHODS

Study Design: This study was designed as a hospital-based cross-sectional study.

Study Period: This study was conducted from June 2023 to May 2024.

Study Setting: The study was conducted in the Department of General Medicine, Government General Hospital (GGH), Guntur.

Study Subjects: A total of 100 male patients admitted with Alcohol Withdrawal Syndrome (AWS) were included in the study.

Inclusion Criteria

Patients fulfilling the following criteria were included in the study:

- Male patients aged more than 21 years
- Patients fulfilling DSM-5 diagnostic criteria for Alcohol Withdrawal Syndrome
- Patients who had abstained from alcohol for a minimum period of 6 hours prior to admission

Exclusion Criteria

The following patients were excluded from the study:

- Patients with a history of seizure disorder
- Patients with neurological disorders predisposing to tremors, nausea, or vomiting
- Patients with history of other substance abuse
- Patients with psychiatric illness associated with hallucinations or delirium
- Patients with chronic renal failure or malabsorption disorders
- Patients receiving diuretics or magnesium supplementation
- Female patients with alcoholism

Study Procedure: After obtaining informed written consent, detailed clinical history including duration of alcohol intake, duration of abstinence, history of alcohol binge, smoking history, and associated comorbidities was recorded using a predesigned proforma. Clinical examination was performed in all patients. Severity of alcohol withdrawal was assessed using the Clinical Institute Withdrawal Assessment for Alcohol-Revised (CIWA-Ar) scale within 6–12 hours of admission.

Venous blood samples were collected under aseptic precautions at admission for biochemical investigations. Serum magnesium levels were estimated by colorimetric method (Xylidyl blue) in the central biochemistry laboratory of GGH, Guntur. The normal reference range for serum magnesium was 1.7–2.2 mg/dL. Laboratory investigations included complete blood picture, liver function tests, renal function tests, serum electrolytes (sodium, potassium, and chloride), viral markers (HBsAg, HCV, and HIV), and serum magnesium levels. Neuroimaging studies were performed whenever clinically indicated.

Statistical Analysis

Data were entered and analyzed using appropriate statistical methods. Continuous variables were expressed as mean ± standard deviation.

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Comparison between groups was performed using Student's t-test and one-way ANOVA. Correlation between CIWA-Ar score and biochemical parameters was assessed using Pearson correlation analysis. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 100 male patients with Alcohol Withdrawal Syndrome (AWS) were included in the study. The majority of patients belonged to the age group of 31–40 years (28%), followed by 41–50 years (27%) and 20–30 years (21%). History of alcohol binge was present in 66% of patients, while 57% had associated smoking history. Hypertension and diabetes mellitus were observed in 28% and 13% of patients respectively.

The duration of alcohol consumption was between 5–10 years in 34% of patients, followed by 10–15 years in 28% and less than 5 years in 27% of patients.

Based on CIWA-Ar scoring, severe withdrawal symptoms (CIWA-Ar score >20) were observed in 58% of patients, whereas 17% had scores between 11–15, 11% had scores between 16–20, and 14% had scores less than 10.

Mean serum magnesium levels showed a statistically significant decline with increasing severity of alcohol withdrawal. Patients with CIWA-Ar score <10 had a mean serum magnesium level of 1.95 ± 0.16 mg/dL, whereas patients with CIWA-Ar score >20 had a mean level of 0.71 ± 0.35 mg/dL ($p<0.001$). Similarly, serum potassium levels also demonstrated significant reduction with increasing withdrawal severity ($p<0.001$). Serum creatinine showed a statistically significant association with CIWA-Ar severity groups ($p=0.041$), while serum sodium and serum urea did not show significant association.

Patients with higher CIWA-Ar scores had significantly longer duration of alcohol intake compared to those with lower scores (10.35 ± 4.09 years vs 7.22 ± 4.57 years, $p=0.001$).

Pearson correlation analysis demonstrated a strong negative correlation between CIWA-Ar score and serum magnesium levels ($r = -0.808$, $p<0.001$). Serum potassium levels also showed significant negative correlation with CIWA-Ar score ($r = -0.693$, $p<0.001$). Duration of alcohol intake showed a significant positive correlation with withdrawal severity ($r = 0.406$, $p=0.001$). Serum creatinine demonstrated weak positive correlation with CIWA-Ar score ($r = 0.236$, $p=0.018$).

Patients with serum magnesium levels below 0.5 mg/dL had the highest mean CIWA-Ar score (46.69 ± 3.94), whereas patients with serum magnesium levels between 1.71–2.3 mg/dL had the lowest mean CIWA-Ar score (10.85 ± 7.89). This association was statistically significant ($p<0.001$).

Table 1: Baseline Characteristics of Study Population

Variable	Frequency (%)
Age 20-30 Years	21 (21%)
Age 31-40 Years	28 (28%)
Age 41-50 Years	27 (27%)
Age 51-60 Years	18 (18%)
Age >60 Years	6 (6%)
History of Alcohol binge drinking	66 (66%)
Smoking history	57 (57%)
Diabetes Mellitus	13 (13%)
Hypertension	28 (28%)

Table 2: Distribution of CIWA-Ar Severity Scores

CIWA-Ar Score	Frequency (%)
<10	14 (14%)
11-15	17 (17%)
16-20	11 (11%)
>20	58 (58%)

Table 3: Mean Serum Magnesium Levels According to CIWA-Ar Severity

CIWA-Ar Score	Mean Serum Magnesium (mg/dL) ±SD
<10	1.95 ± 0.16
11-15	1.56 ± 0.31
16-20	1.54 ± 0.19
>20	0.71 ± 0.35

One-way ANOVA, $p < 0.001$.

Table 4: Correlation of CIWA-Ar Score with Clinical and Biochemical Parameters

Parameter	Correlation Coefficient (r)	p-Value
Serum Magnesium	-0.808	<0.001
Serum Potassium	-0.693	<0.001
Serum Sodium	-0.243	0.015
Serum Creatinine	0.236	0.018
Duration of Alcohol Intake	0.406	0.001

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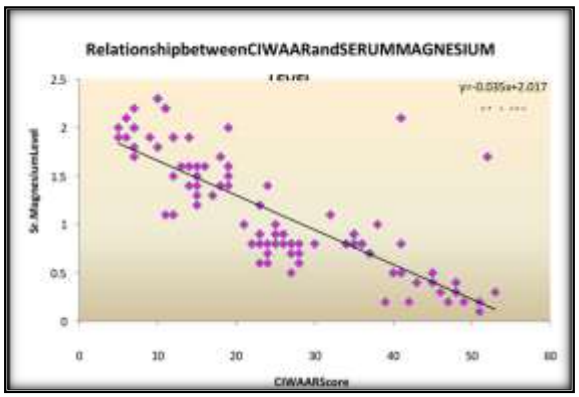

Figure 1: Relationship between CIWA-Ar Score and Serum Magnesium Levels

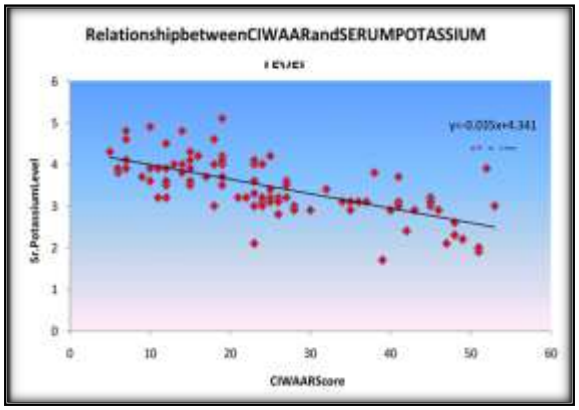

Figure 2: Relationship between CIWA-Ar Score and Serum Potassium Levels

DISCUSSION

The present study demonstrated a significant inverse association between serum magnesium levels and the severity of Alcohol Withdrawal Syndrome (AWS). Mean serum magnesium levels progressively declined with increasing CIWA-Ar scores, and a strong negative correlation was observed between serum magnesium levels and withdrawal severity ($r = -0.808$, $p<0.001$). In addition, serum potassium levels were significantly lower among patients with severe withdrawal symptoms. These findings suggest that hypomagnesemia and associated electrolyte disturbances are closely related to the clinical severity of alcohol withdrawal.

Our findings are consistent with those reported by Vanoni et al., who demonstrated significantly reduced circulating magnesium levels in patients with chronic alcohol use disorder and highlighted the high prevalence of magnesium deficiency in this population.[3] Similarly, Qureshi et al. observed that lower serum magnesium and potassium levels were associated with greater severity of alcohol withdrawal syndrome, supporting the role of these biochemical parameters as objective markers of withdrawal severity.[14] Ayirolimeethal et al. also reported a significant association between lower serum magnesium levels and increased severity of alcohol withdrawal manifestations, further supporting the observations of the present study.[13]

The association between hypomagnesemia and severe alcohol withdrawal may be explained by the important role of magnesium in neuromuscular transmission and regulation of neuronal excitability. Chronic alcohol consumption promotes magnesium depletion through poor nutritional intake, gastrointestinal losses, and increased renal excretion.[5,6] Reduced magnesium levels may enhance neuronal hyperexcitability and contribute to severe withdrawal manifestations. Therefore, routine assessment of serum magnesium may serve as a useful adjunct in identifying patients at risk of severe AWS and facilitate timely corrective management. Although current evidence does not support routine magnesium supplementation solely for the treatment of AWS, early identification and correction of hypomagnesemia may help reduce complications associated with severe withdrawal.[12]

Limitations

This study was conducted at a single tertiary care center and included only male patients, which may limit the generalizability of the findings. The cross-sectional design precludes establishing a causal relationship between serum magnesium levels and withdrawal severity. In addition, factors such as nutritional status, severity of liver disease, and intracellular magnesium levels were not assessed.

CONCLUSION

The present study demonstrated a significant inverse relationship between serum magnesium levels and the severity of Alcohol Withdrawal Syndrome. Patients with severe withdrawal symptoms had markedly lower serum magnesium levels, and serum magnesium showed a strong negative correlation with CIWA-Ar scores. These findings suggest that hypomagnesemia is common among patients with AWS and may serve as a useful biochemical marker of withdrawal severity. Routine assessment of serum magnesium levels at admission may help identify high-risk patients and facilitate appropriate monitoring and supportive management. Further prospective studies are required to evaluate whether early correction of hypomagnesemia improves clinical outcomes in Alcohol Withdrawal Syndrome.

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