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Critical Care Illness Polyneuropathy in ICU Patients on Mechanical Ventilation

Lamat Un Noor[1], Prashant Sudam Dhumal[2]

[1]Assistant Professor, Department of Medicine, Govt. Medical College and Hospital, Chhatrapati Sambhajinagar (Aurangabad), Maharashtra 431004, India.
[2]Assistant Professor, Department of Medicine, Govt. Medical College and Hospital, Chhatrapati Sambhajinagar (Aurangabad), Maharashtra 431004, India.

Corresponding Author: Lamat Un Noor

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ABSTRACT

Introduction: Critical illness polyneuropathy (CIP) is an important neuromuscular complication of severe critical illness and prolonged mechanical ventilation. It may contribute to difficulty in weaning, prolonged ICU stay, and adverse clinical outcomes. This study evaluated the incidence of CIP and its association with clinical factors and outcomes in mechanically ventilated ICU patients.
Materials and Methods: A prospective observational study was conducted among 150 adult ICU patients requiring mechanical ventilation. Demographic and clinical characteristics, APACHE II and SOFA scores, sepsis, septic shock, corticosteroid and neuromuscular blocker exposure, VAP, duration of mechanical ventilation and weaning, reintubation, tracheostomy, ICU and hospital stay, and mortality were assessed. CIP was diagnosed using electrophysiological nerve conduction and electromyographic findings. Patients with and without CIP were compared using appropriate statistical tests, with $p<0.05$ considered statistically significant.
Results: CIP was identified in 52 (34.7%) patients. Sepsis (80.8% vs. 62.2%, p=0.02), septic shock (46.2% vs. 23.5%, p=0.005), higher APACHE II and SOFA scores ($p<0.001$), corticosteroid use (p=0.01), neuromuscular blocker use (p=0.04), and VAP (p=0.04) were significantly associated with CIP. CIP was associated with longer mechanical ventilation and weaning duration ($p<0.001$), higher weaning failure, reintubation and tracheostomy rates, and prolonged ICU and hospital stay ($p<0.001$). Mortality was higher but not statistically significant.
Conclusion: CIP was frequent among mechanically ventilated ICU patients and was associated with greater illness severity, prolonged ventilatory support, difficult weaning, and longer ICU and hospital stay.
Keywords: Critical illness polyneuropathy; Mechanical ventilation; Sepsis; Weaning failure; Intensive care unit.

INTRODUCTION

Critically ill patients frequently develop complications that can persist beyond the resolution of the primary illness and substantially delay recovery. Among these, neuromuscular abnormalities are increasingly recognized as important complications, particularly in patients with

severe systemic illness who require prolonged intensive care and mechanical ventilation. [1] These abnormalities may involve both the peripheral nerves and skeletal muscles and can result in significant generalized weakness, impaired physical function, and difficulty in liberation from ventilatory support. [2]

Critical illness polyneuropathy (CIP) is one of the most well-characterized neuromuscular disorders associated with critical illness. It is predominantly observed in patients with severe sepsis, septic shock, multiorgan dysfunction, and prolonged ICU stays. [3] The condition is characterized by diffuse weakness resulting from dysfunction of peripheral motor and sensory nerves. Its clinical recognition may be challenging because weakness in critically ill patients can have several contributing causes, including prolonged immobilization, sedation, metabolic abnormalities, myopathy, and the underlying systemic disease. [4]

An important clinical manifestation of CIP is difficulty in weaning from mechanical ventilation. Patients may remain dependent on ventilatory support despite improvement in the primary cause of respiratory failure because generalized neuromuscular weakness can impair respiratory muscle function. [5,6] Previous studies have reported an association between CIP and prolonged mechanical ventilation; however, the findings have not been consistent. Some investigations have demonstrated longer periods of ventilation and weaning among patients with CIP, whereas others have not observed a significant difference. [6] This variation raises an important question as to whether CIP itself contributes independently to prolonged ventilatory dependence or whether the observed association is primarily related to other factors commonly present in critically ill patients. [7]

The development of CIP may also have consequences extending beyond ventilator dependence. Persistent neuromuscular weakness can interfere with mobilization and rehabilitation and may contribute to prolonged ICU or hospital stay. [8] Furthermore, the additional requirement for intensive care and rehabilitation may increase healthcare utilization and treatment-related costs. However, the independent effect of CIP on hospital outcomes remains incompletely established, particularly among patients who have survived the acute phase of critical illness and have reached the stage of attempted ventilator weaning. [9]

Patients with severe sepsis or septic shock who require prolonged mechanical ventilation represent a population at considerable risk of developing critical illness–associated neuromuscular weakness. [9,10] Evaluating these patients at the stage when the underlying acute illness has improved and they are considered suitable for discontinuation of mechanical ventilation provides an opportunity to better determine the clinical significance of CIP. Assessment at this stage may help distinguish the consequences of neuromuscular dysfunction from those attributable to ongoing critical illness. [9-11]

Therefore, the present study is designed to prospectively evaluate critical illness polyneuropathy in mechanically ventilated patients with severe sepsis or septic shock. The study will primarily assess whether the presence of CIP is associated with prolonged mechanical ventilation after considering other factors that may influence weaning. It will additionally evaluate its relationship with duration of hospital stay and healthcare costs. Understanding these associations may help in the early recognition of CIP, appropriate rehabilitation planning, and improved management of patients recovering from severe critical illness.

MATERIAL & METHODS

The present prospective observational study was conducted among adult ICU patients with severe sepsis or septic shock who required mechanical ventilation for ≥7 days and were considered clinically ready for weaning. 150 patients aged <18 years, pregnant patients, those intubated for COPD exacerbation, and those with pre-existing neuromuscular disease, liver cirrhosis, end-

stage renal disease, or HIV infection were excluded.

Patients were assessed daily for readiness for weaning based on clinical stability, adequate oxygenation, temperature <38°C, hemoglobin ≥9 g/dL, and ability to follow commands. Weaning was initiated with a 2-hour spontaneous breathing trial using a T-piece, followed by progressive reduction of pressure support when required.

Demographic data, APACHE II and SOFA scores, duration of mechanical ventilation, sedative and muscle relaxant exposure, comorbidities, ventilator-associated pneumonia, ICU stay, hospital stay, reintubation, tracheostomy, and mortality were recorded.

At the onset of weaning, all patients underwent nerve conduction studies and needle electromyography. Motor and sensory nerve conduction and evidence of denervation were assessed. CIP was diagnosed by electrophysiological evidence of an acute axonal neuropathy characterized by reduced motor and sensory action potential amplitudes with relatively preserved conduction velocities and distal latencies, along with denervation changes.

Patients were divided into CIP and non-CIP groups and compared for duration of mechanical ventilation, weaning outcomes, ICU/hospital stay, and mortality.

Continuous variables were analyzed using the student's t-test or Mann–Whitney U test, while categorical variables were compared using the chi-square or Fisher's exact test. A two-sided p-value <0.05 was considered statistically significant.

RESULTS

A total of 150 mechanically ventilated ICU patients fulfilling the predefined eligibility criteria were included in the study. The demographic characteristics, clinical profile, severity of illness, and incidence of critical illness polyneuropathy (CIP) were assessed. Patients with and without CIP were subsequently compared with respect to risk factors, duration of mechanical ventilation, weaning outcomes, ICU stay, hospital stay, and mortality.

Among the 150 mechanically ventilated ICU patients, the mean age was 56.8 ± 15.2 years, with males comprising 62.7% and females 37.3%. The mean BMI was 24.9 ± 4.1 kg/m², while diabetes mellitus was present in 34.0% of patients. Sepsis was observed in 68.7%, including 31.3% with septic shock. The mean APACHE II and SOFA scores were 19.6 ± 5.7 and 8.2 ± 2.9, respectively. Ventilator-associated pneumonia occurred in 28.0% of patients. (Refer Table 1)

Table 1: Baseline characteristics of study participants (n=150)

Variable	Total (n=150)
Age (years), mean ± SD	56.8 ± 15.2
Male, n (%)	94 (62.7)
Female, n (%)	56 (37.3)
BMI (kg/m²), mean ± SD	24.9 ± 4.1
Diabetes mellitus, n (%)	51 (34.0)
Sepsis, n (%)	103 (68.7)
Septic shock, n (%)	47 (31.3)
APACHE II score, mean ± SD	19.6 ± 5.7
SOFA score, mean ± SD	8.2 ± 2.9
Ventilator-associated pneumonia, n (%)	42 (28.0)

Among the 150 mechanically ventilated ICU patients, critical illness polyneuropathy (CIP) was identified in 52 (34.7%) patients, while 98 (65.3%) patients did not develop CIP. Thus, approximately one-third of the study population demonstrated electrophysiological evidence of CIP. (Refer figure 1)

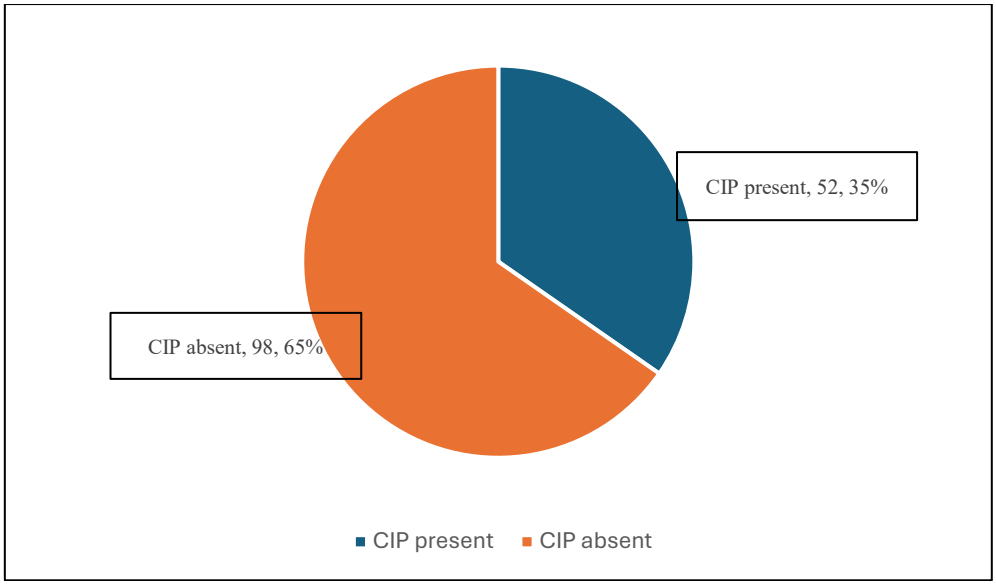


Figure 1 - Incidence of critical illness polyneuropathy

Comparison of patients with and without CIP showed that sepsis (80.8% vs. 62.2%, p=0.02) and septic shock (46.2% vs. 23.5%, p=0.005) were significantly more frequent in the CIP group. Patients with CIP also had significantly higher APACHE II and SOFA scores (p<0.001 for both). Corticosteroid use, neuromuscular blocker use, and ventilator-associated pneumonia were also significantly more common among patients with CIP (p=0.01, 0.04, and 0.04, respectively). Age and diabetes mellitus did not show a statistically significant difference between the two groups. (Refer Table 2)

Table 2: Comparison of risk factors and severity between CIP and non-CIP groups

Variable	CIP (n=52)	Non-CIP (n=98)	p-value
Age (years)	59.4 ± 14.8	55.4 ± 15.3	0.12
Diabetes, n (%)	22 (42.3)	29 (29.6)	0.11
Sepsis, n (%)	42 (80.8)	61 (62.2)	**0.02**
Septic shock, n (%)	24 (46.2)	23 (23.5)	**0.005**
APACHE II score	22.1 ± 5.4	18.3 ± 5.4	**<0.001**
SOFA score	9.4 ± 2.7	7.6 ± 2.8	**<0.001**
Corticosteroid use, n (%)	34 (65.4)	42 (42.9)	**0.01**
Neuromuscular blocker use, n (%)	19 (36.5)	20 (20.4)	**0.04**
VAP, n (%)	20 (38.5)	22 (22.4)	**0.04**

Patients with CIP had a significantly longer duration of mechanical ventilation than those without CIP (18.7 ± 7.1 vs. 11.8 ± 5.1 days, p<0.001). The duration of weaning was also significantly prolonged in the CIP group (6.2±3.4 vs. 3.5±2.1 days, p<0.001). Furthermore, weaning failure (38.5% vs. 17.3%, p=0.005), reintubation (26.9% vs. 13.3%, p=0.04), and tracheostomy (30.8% vs. 13.3%, p=0.01) were significantly more frequent among patients with CIP. These findings indicate that CIP was associated with more difficult and prolonged liberation from mechanical ventilation. (Refer Table 3)

Table 3: Association of CIP with mechanical ventilation and weaning outcomes

Outcome	CIP (n=52)	Non-CIP (n=98)	p-value
Duration of mechanical ventilation (days)	18.7 ± 7.1	11.8 ± 5.1	**<0.001**
Duration of weaning (days)	6.2 ± 3.4	3.5 ± 2.1	**<0.001**
Weaning failure, n (%)	20 (38.5)	17 (17.3)	**0.005**
Reintubation, n (%)	14 (26.9)	13 (13.3)	**0.04**
Tracheostomy, n (%)	16 (30.8)	13 (13.3)	**0.01**

Patients with CIP had significantly longer ICU stay than those without CIP (23.4 ± 8.7 vs. 16.1 ± 6.4 days, p<0.001). Similarly, hospital stay was significantly prolonged in the CIP group (31.2 ± 11.0 vs. 22.3 ± 8.7 days, p<0.001). Although ICU mortality (23.1% vs. 12.2%) and hospital mortality (26.9% vs. 15.3%) were higher among patients with CIP, the differences were not statistically significant (p=0.09 for both).

DISCUSSION

The present study evaluated 150 mechanically ventilated ICU patients and identified critical illness polyneuropathy (CIP) in 52 (34.7%) patients. The mean age of the study population was 56.8 ± 15.2 years, with a male predominance (62.7%). Diabetes mellitus was present in 34.0% of patients, while sepsis and septic shock were present in 68.7% and 31.3%, respectively. The mean APACHE II and SOFA scores were 19.6 ± 5.7 and 8.2 ± 2.9, respectively, indicating a substantially ill ICU population. VAP was observed in 28.0% of patients. These characteristics are consistent with the clinical setting in which CIP is most frequently described, particularly among patients with sepsis, severe systemic inflammation, organ dysfunction and prolonged mechanical ventilation. Bolton and colleagues initially described CIP as an acute axonal neuropathy associated with severe critical illness and sepsis, while De Jonghe et al. [7] subsequently identified severity of illness and systemic inflammatory response as important determinants of ICU-acquired neuromuscular dysfunction.

In the present study, CIP was detected in 34.7% of mechanically ventilated patients. This finding is comparable with the 33% incidence of critical illness polyneuropathy/myopathy reported by De Jonghe et al. among mechanically ventilated critically ill patients. A systematic review by Stevens et al. reported neuromuscular dysfunction acquired in critical illness in approximately 46% of ICU patients with sepsis, multiple organ failure or prolonged mechanical ventilation; however, the authors emphasized heterogeneity in diagnostic criteria and difficulty in distinguishing isolated neuropathy from myopathy. Garnacho-Montero et al. [1] reported a higher incidence of CIP (53.1%) in patients with severe sepsis or septic shock requiring mechanical ventilation for at least 7 days. The comparatively lower incidence in the present study may be related to differences in patient selection, severity of illness, duration of mechanical ventilation and electrophysiological diagnostic criteria.

Age was not significantly different between patients with and without CIP in the present study (59.4 ± 14.8 vs. 55.4 ± 15.3 years; p=0.12). Similarly, De Jonghe et al. [7] did not identify age as a consistent determinant of ICU-acquired neuromuscular dysfunction, and systematic review data have not demonstrated a consistent association between age and CIP/CIM. Thus, the development of CIP in the present cohort appears to be more closely related to the severity and characteristics of critical illness than to age alone.

Diabetes mellitus was more frequent among patients with CIP than among those without CIP (42.3% vs. 29.6%), although the difference did not reach statistical significance (p=0.11). Previous literature has identified diabetes and metabolic disturbances as potential risk factors for ICU-acquired neuromuscular dysfunction.

Sepsis was significantly more common in patients who developed CIP than in those without CIP (80.8% vs. 62.2%, p=0.02), while septic shock was also significantly more frequent (46.2% vs. 23.5%, p=0.005). These findings support the established relationship between systemic inflammation, sepsis and development of ICU-acquired neuromuscular dysfunction**.** Bolton et al [12] proposed an association between severe sepsis and acute axonal nerve injury, while De Jonghe et al. [7] demonstrated that the systemic inflammatory response and severity of illness were important predictors of CIP/CIM. Latronico et al [5] similarly identified sepsis, systemic inflammatory response and multiple organ failure as major

risk factors.

The present study demonstrated significantly higher APACHE II scores among patients with CIP compared with non-CIP patients (22.1 ± 5.4 vs. 18.3 ± 5.4; p<0.001). Similarly, SOFA scores were significantly higher in the CIP group (9.4 ± 2.7 vs. 7.6 ± 2.8; p<0.001). These findings indicate that greater severity of acute illness was associated with development of CIP. De Jonghe et al. [7] reported that APACHE III score was significantly associated with the development of critical illness polyneuropathy/myopathy and suggested that severity of illness, together with systemic inflammation, could be used to identify patients at increased risk. In another cohort, Garnacho-Montero et al. [1] found CIP in patients with severe sepsis/septic shock and demonstrated its association with prolonged ventilatory support and weaning difficulty.

Corticosteroid exposure was significantly more frequent in the CIP group than in the non-CIP group (65.4% vs. 42.9%, p=0.01). Historically, corticosteroids have been implicated in ICU-acquired neuromuscular weakness, particularly in combination with prolonged neuromuscular blockade.

Neuromuscular blocker use was also significantly higher among patients with CIP (36.5% vs. 20.4%, p=0.04). This finding is consistent with some earlier observational studies; for example, Leijten et al. identified neuromuscular blocking agents as an independent risk factor for CIP/CIM. Ventilator-associated pneumonia was significantly more common among patients with CIP than among those without CIP (38.5% vs. 22.4%, p=0.04). This finding is clinically relevant because VAP may prolong mechanical ventilation and increase systemic inflammatory burden, thereby creating conditions associated with ICU-acquired neuromuscular dysfunction.

A major finding of the present study was the significantly longer duration of mechanical ventilation among patients with CIP compared with those without CIP (18.7 ± 7.1 vs. 11.8 ± 5.1 days; p<0.001). This finding is strongly supported by previous studies. Garnacho-Montero et al. [1] reported significantly longer mechanical ventilation among septic patients with CIP, with a median duration of 34 versus 14 days (p<0.001).

The duration of weaning was also significantly longer in the CIP group (6.2 ± 3.4 vs. 3.5 ± 2.1 days; p<0.001). Garnacho-Montero et al. [1] demonstrated a similar association, reporting a median weaning duration of 15 days in patients with CIP compared with 2 days in those without CIP. Weaning failure occurred significantly more frequently in patients with CIP than in non-CIP patients (38.5% vs. 17.3%, p=0.005).

Reintubation was significantly more common in the CIP group than in the non-CIP group (26.9% vs. 13.3%, p=0.04). Similarly, tracheostomy was performed more frequently among patients with CIP (30.8% vs. 13.3%, p=0.01). These findings are likely related to the prolonged ventilatory requirement and difficulty achieving successful liberation from mechanical ventilation among patients with ICU-acquired weakness.

Patients with CIP had a significantly longer ICU stay than patients without CIP (23.4 ± 8.7 vs. 16.1 ± 6.4 days; p<0.001). Hospital stay was also significantly longer in the CIP group (31.2 ± 11.0 vs. 22.3 ± 8.7 days; p<0.001). These findings are in agreement with previous literature. Leijten et al. [13] reported longer ICU and hospital stays among patients who developed CIP.

Although ICU mortality was higher in patients with CIP than in those without CIP (23.1% vs. 12.2%), this difference was not statistically significant (p=0.09). Similarly, hospital mortality was numerically higher in the CIP group (26.9% vs. 15.3%), but the difference did not reach statistical significance (p=0.09).

Overall, the present study demonstrates that CIP is a relatively frequent complication among mechanically ventilated ICU patients and is particularly associated with sepsis, septic shock and greater severity of acute illness as reflected by APACHE II and SOFA

scores. CIP was also associated with corticosteroid and neuromuscular blocker exposure and VAP, although these treatment-related associations should not be interpreted as causal. Most importantly, patients with CIP experienced prolonged mechanical ventilation and weaning, higher rates of weaning failure, reintubation and tracheostomy, and significantly longer ICU and hospital stays. Although mortality was numerically higher among patients with CIP, the difference was not statistically significant. These findings emphasize the importance of early recognition of ICU-acquired neuromuscular dysfunction, particularly in patients with severe sepsis, septic shock and prolonged or difficult weaning.

Limitations of this Study

The study was conducted at a single tertiary-care centre, which may limit the generalizability of the findings to other ICU settings and patient populations. The relatively small sample size of 150 patients may have limited the statistical power to detect associations, particularly for mortality outcomes. CIP was assessed using electrophysiological studies at the onset of weaning; therefore, the exact timing of onset of neuropathy during the ICU stay could not be determined.

CONCLUSION

Critical illness polyneuropathy was identified in 34.7% of mechanically ventilated ICU patients in the present study. CIP was significantly associated with sepsis, septic shock, higher APACHE II and SOFA scores, corticosteroid and neuromuscular blocker use, and VAP. Patients with CIP had significantly longer mechanical ventilation and weaning durations, with higher rates of weaning failure, reintubation, and tracheostomy. They also had significantly prolonged ICU and hospital stays. Although ICU and hospital mortality were higher in patients with CIP, the differences were not statistically significant. Early recognition of CIP, particularly in patients with severe critical illness and difficult weaning, may help in anticipating prolonged ventilatory support and ICU stay.

Declaration

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Conflict of Interest: The authors declare no conflict of interest.

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