

Evaluation of Sleep Architecture Using 24-hour Polysomnography in Patients Recovering from Critical Illness in an Intensive Care Unit and High Dependency Unit: A Longitudinal, Prospective, and Observational Study

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ABSTRACT

Background and objective: The sleep architecture of critically ill patients being treated in Intensive Care Units (ICU) and High Dependency Units (HDU) is frequently unsettled and inadequate both qualitatively and quantitatively. The study aimed to investigate and elucidate factors influencing sleep architecture and quality in ICU and HDU in a limited resource setting with financial constraints, lacking human resources and technology for routine monitoring of noise, light and sleep promotion strategies in ICU. Methods: The study was longitudinal, prospective, hospital-based, analytic, and observational. Insomnia Severity Index (ISI) and the Epworth Sleepiness Scale (ESS) pre hospitalisation scores were recorded. Patients underwent 24-hour polysomnography (PSG) with the simultaneous monitoring of noise and light in their environments. Patients stabilised in ICU were transferred to HDU, where the 24-hour PSG with the simultaneous monitoring of noise and light in their environments was repeated. Following PSG, the Richards-Campbell Sleep Questionnaire (RCSQ) was employed to rate patients' sleep in both the ICU and HDU. Results: Of 46 screened patients, 26 patients were treated in the ICU and then transferred to the HDU. The mean (SD) of the study population's mean (SD) age was 35.96 (11.6) years with a predominantly male population (53.2% (n=14)). The mean (SD) of the ISI and ESS scores were 6.88 (2.58) and 4.92 (1.99), respectively. The comparative analysis of PSG data recording from the ICU and HDU showed a statistically significant reduction in N1, N2 and an increase in N3 stages of sleep (p<0.05). Mean (SD) of RCSQ in the ICU and the HDU were 54.65 (7.70) and 60.19 (10.85) (p-value = 0.04) respectively. The disease severity (APACHE II) has a weak correlation with the arousal index but failed to reach statistical significance (coeff= 0.347, p= 0.083). Conclusion: Sleep in ICU is disturbed and persisting during the recovery period in critically ill. However, during recovery, sleep architecture shows signs of restoration.

Keywords: sleep deprivation, sleep stages, polysomnography, sleep disorders

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INTRODUCTION

Sleep disturbance is defined as the perceived or actual alterations in nighttime sleep (both quantity and quality) with the subsequent daytime impairment of quality of life. Sleep in critically ill patients in the ICU remains qualitatively and quantitatively insufficient [1]. The patient's total sleep time is normally 7-9 hrs. However, sleep is highly fragmented, with six to seven awakenings per hour. In one study, the median duration of sleep without awakening is has been reported to be three minutes [2], with almost 50% of the patient's total sleep time occurring during daylight hours [3].

In critically ill patients, polysomnography (PSG) data demonstrate that stage N1, which occurs right after one falls asleep, is very short-lasting less than 10 minutes, and stage N2 lasts for 30 to 60 minutes, predominates with limited restorative benefits. Correspondingly, there is a reduction of rapid eye movement (REM) sleep and slow-wave sleep (SWS) [3]. Sleep disturbance can persist for months after discharge [4].

Factors contributing to poor sleep are severity of the illness, environmental noise, light intensity, types and modes of mechanical ventilation, and drugs [1, 5].

Often, patients admitted to an ICU are not discharged directly but transferred to a HDU, depending upon their consciousness level and hemodynamic stability. Sleep data on patients in high dependency units or similar environment is limited [6]. Cooper et al. (2000) demonstrated an increased number of arousals associated with noise in an intermediate respiratory care unit (IRCU) during nighttime polysomnography [6].

Sleep deprivation's clinical consequences result in alterations in immune function, homeostatic mechanisms, respiratory muscle functions, and neurocognitive impairment.

The current study aimed to detect and elucidate factors influencing the quality and quality of sleep deprivation and sleep architecture of life in ICU and HDU in a limited resource setting.

The study was a longitudinal, prospective, hospitalbased observational study was conducted in an adult ICU (14) and HDU (22) of the Department of Pulmonary and Critical Care Medicine of the Pt. BD.Sharma Post Graduate Institute of Medical Sciences, Rohtak, India. The study had the approval of the ethical committee of the university.

The ICU provided speciality services such as pulmonary, neuro and gastro critical care. It was a closed unit with an accredited Intensivist in charge of all patients. Ward rounds were conducted by the intensivist twice a day when treatment goals and treatment plans were assessed.

A registered nurse executed all the nursing care for the patient. The registered nurse to patient ratio was 1:3 for mechanically ventilated patients and 1:5 for patients requiring high dependency care. There was a separate high dependency ward. The sleep-promoting habits were dimming of lights during nighttime.

Patients admitted to the ICU were evaluated for the study.

The inclusion criteria were: patients aged 18 - 70 years, admission \ge 24hrs who willing signed informed consent.

The exclusion criteria were: comatose, delirious, or agitated patients requiring pharmacological interventions, neurological diseases or neurotrauma, preexisting sleep disorders, psychiatric disorders, and not giving signed informed consent.

If the patient could not sign the consent form, the form was signed or refused by their next of kin.

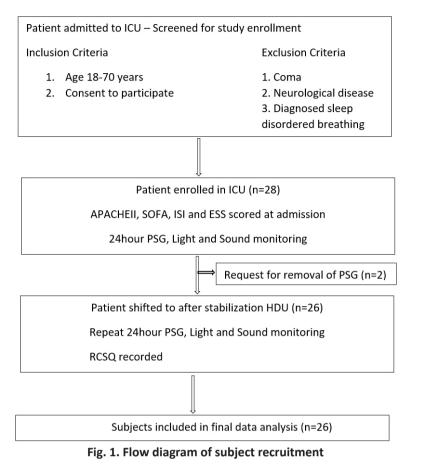
The Flow diagram showing subject recruitment is given in Figure 1.

The study was conducted over one year from 01.08.2015 to 01.08.2016

On admission, the demographic and clinical data were recorded in the patient's ICU record. The APACHE II (Acute physiology and chronic health evaluation) score and SOFA (Sequential Organ Failure Assessment) at the time of enrolment were both calculated to assess the severity of illness.

Once enrolled on the study, patients rated their sleep quality before hospitalisation using a 1 to 10 scale, and patients or their proxy completed the validated Insomnia Severity Index [7]. The Epworth Sleepiness Scale was used to rate pre hospitalisation daytime sleepiness [8]. The Richmond agitation and sedation scale were used to assess the patient's sedation and calmness before the polysomnography data were acquired [9].

When hemodynamic stability and reversal of cause of ventilatory support had been achieved and cessation of sedation with benzodiazepine and neuro-muscular blocking agents for at least 72 hours, patients under-



went 24-hour polysomnography with simultaneous monitoring of noise and light.

However, if required, patients on mechanical ventilation were given opioids and benzodiazepines 1mg/mL, 25µg, i.v., fentanyl (NEON, Pharmaceuticals, Mumbai, India) 1.g/mL, 1mg, i.v. Midazolam (VHB Medicals, Uttarakhand, India) to maintain comfort during the polysomnography recording. The opioids were given to mechanically ventilated patients only.

After stabilisation and recovery in ICU, the patients were transferred to a high dependency unit, where the polysomnography data gathering was repeated.

The time gap between the two polysomnography parts of the study was at least seven days. Richards-Campbell Sleep Questionnaire was employed to rate patients' sleep in both the ICU and high dependency units on the day following completion of the polysomnography.

Polysomnography Study

The Level-2, 24-hour polysomnography study was done using the ALICE PDx device (Alice PDX; Philips Respironics, Murrysville, PA, USA.)

The recording was started and finished between the hours of 9 am and 6 pm.

The gold cup Electroencephalograph electrodes were placed at the left occipital (O1), right mastoid (M2), right central (C4) and left mastoid (M1) according to the International 10-20 System [10]. The electromyography electrodes were located over the right and left masseter muscles. The electrooculography electrodes on the left side were placed below the outer canthus, and the right was placed above the outer canthus. A single electrocardiograph electrode (Lead II) was placed for recording.

Electrode impedance was maintained at <10,000 ohms. Visual checks were performed two hourly, and electrodes were replaced if impedance values approached 10,000 ohms or when the patient was disturbed for routine reposition. Polysomnography recordings were scored manually in 30-second epochs using standard Rechtschaffen and Kales criteria [11]. Total sleep time was defined as the time spent in all sleep stages. Scoring of arousal and arousal index was scored using the American Academy of Sleep Medicine manual [11]. The sleep stage nomenclature was scored

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using the Wake (Stage W), Non-Rapid Eye Movement (Stage N1, Stage N2, Stage N3) and Rapid Eye Movement (Stage R).

The light and sound levels were recorded simultaneously during both parts of the polysomnography study.

Illuminance level (lux) was recorded using a sensor placed close to the patient's head, once per 30 minutes, using a Lux meter (Sigma instruments, model number 1010A, New Delhi, India).

The ICU had no natural light provision, while in the high dependency units, glass windows were situated near each bed, allowing sunlight exposure during the daytime. The primary practice associated with sleep promotion was dimming the main lights after 11 pm. Sound levels were recorded using the 'A' weighted sound level meter (Sigma instruments, model number MS6708, New Delhi, India) once every 30 minutes.

Patients were monitored for one 24-hour period using an ALICE PDx device (Alice PDX; Philips Respironics, Murrysville, PA, USA.), and all recordings began and finished between 1000 and 1700 hours. Electroencephalograph (EEG) (O1/M2, C4/M1), electromyograph , electro-oculograph , (right and left) and electrocardiograph (lead II) were recorded.

The patient's skin was prepared according to standard techniques. Gold cup EEG electrodes were placed at O1/M2 and C4/M1 according to the International 10-20 System [12]. Two EOG electrodes were used for right and left eye movements. The EMG electrodes were located over the right and left masseter (facial) muscles. Electrode application was performed by the authors (RE and MF), who were trained in the technique. Electrode impedance was maintained at <9,000 ohms. Visual checks were performed hourly, and electrodes were replaced if impedance values approached 9,000 ohms or when the patient was disturbed for routine repositioning.

Sound and illuminance levels were recorded simultaneously with PSG using the integrated sound pressure level meter (Sigma instruments, model number MS6708, New Delhi, India) illuminance level meter (Sigma instruments, model number 1010A, New Delhi, India)

Continuous equivalent sound pressure levels (Leq) in 'A' weighted decibels and peak sound pressure levels (Speak) in 'C' weighted decibels were logged every second.

Illuminance level, in lux, was recorded using a sensor placed close to the patient's head once per minute. The nurse was requested to log an event whenever the patient received treatment or care using a computer within reach.

The log data contained the following items: clinical assessment; tracheal suctioning; pressure area care; physiotherapy; mouth/eye care; blood test (sampling); wash; noninvasive blood pressure; eating and drinking; dressing; pain; line insertion; X-ray; clinical crisis; agitation/anxiety/confusion; electrode replacement.

Upon completing polysomnography recording, patients rated their previous night's sleep using the Richards Campbell Sleep Questionnaire. This contains five 100mm visual analogue scales (VAS): sleep depth, latency, awakenings, time awake and quality of sleep, with higher scores indicating better sleep.

Three to ten days after being transferred to the ward, patients rated their sleep using the Richards Campbell Sleep Questionnaire. They also reported on sleep-disturbing factors in the ICU using the Sleep in Intensive Care Questionnaire. This comprises seven questions (rated 1 to 10), including overall sleep quality at home, sources of perceived sleep disruption, and noise sources.

Polysomnography recordings were scored manually in 30-second epochs using standard Rechtschaffen and Kales criteria [11]. Total sleep time was defined as the time spent in all sleep stages. Scoring of arousal and arousal index was scored using the American Academy of Sleep Medicine manual [11]. The sleep stage nomenclature was scored using the Wake (Stage W), Non-Rapid Eye Movement (Stage N1, Stage N2, Stage N3) and Rapid Eye Movement (Stage R)

Statistical analysis

The software packages (version 18; SPSS Inc, Chicago, IL, USA) and Microsoft Excel (2007) was used to analyse the data. Means (SD) and medians described continuous data and frequencies and percentages for categorical data. Paired t-test compared the sleep parameters in ICU and high dependency units. Unpaired t-test detected the significance of the difference in the variations of illuminance, noise levels, and nursing care activities in both the ICU and high dependency units environment. Mann-Whitney U test compared sleep parameters in mechanically ventilated versus spontaneously breathing patients, patients taking opioids versus not taking opioids. Pearson correlation analysis established the correlation between several variables and polysomnographic data.

The level of significance was set at p < 0.05.

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Of the 46 screened patients, 28 patients enrolled for participation in the study. Two patients requested removing the PSG after the recording began. Therefore recording data from twenty-six patients in the ICU and subsequently followed up in the HDU were analysed.

Study Population characteristics

The study's demographic, clinical pattern, indications for admission and ICU severity of illness scores are given in Table 1. The mean (SD) on the ISI scoring was 6.88 (2.58). 11(42.3%) patients had subclinical insomnia. The mean (SD) of the ESS was 4.92(1.99). Fifteen patients (57.69%) were on invasive mechanical ventilation (IVM) during the PSG study period, and the mode of ventilation was pressure support ventilation (PSV). One patient was planned for extubation during the PSG study. The mean (SD) of the ICU day on which PSG was done was 5.73 (1.40).

Drugs used for sedation and analgesia during PSG study

50 % of patients in the current study received opioids (fentanyl), and eleven out of thirteen (84%) were on intermittent mandatory ventilation (IMV). However, none of the study population received benzodiazepines, Propofol or dexmedetomidine during PSG recordings. The morphine equivalent dose of opioid was 14.42 microgram/kilogram/hour. Patients were calm and interactive, and the median RASS score was 0 (range -1 to 1).

Arterial Blood Gas Analysis (ABG)

The mean (SD) pH in the ICU and HDU were 7.41 (0.04) and 7.42 (0.025) respectively (p value = 0.48). Only serum potassium level were significantly different in ICU and HDU (3.60 (0.60), 4.1 (0.54):[p value = 0.003)].

FIO2 requirement was reduced in the HDU compared to the ICU (35.19(3.1), 31.46(2.3): p value= 0.06).

Comparison of PSG data of ICU and HDU

The comparative analysis of PSG data recording from the ICU and HDU are presented in Table 2. The statistically significant reduction in N1, N2, and correspondingly increase in N3 stages of sleep was documented. Notably, a statistically significant reduction was seen in the mean arousal index (AI) in the HDU compared to the ICU (22.65 (10.49), 16.55(5.15): p = 0.006). The mean duration of sleep without wake improved in the HDU compared to the ICU (3.18 (1.35) minutes, 4.01(1.39) minutes, respectively (p = 0.03). RCSQ was assessed the day following PSG in the ICU and the HDU. The RCSQ, mean (SD), in the ICU was 54.65 (7.69) and in the HDU was 60.19(10.85) (p-value = 0.04).

Effect of Light and Noise

The comparative analysis of Light (illuminance) and Sound (decibels) presented in Table 3 and Figure 2a, b, and 3a, b. The mean illuminance difference between day and night in the ICU and the HDU was statistically significant (p<0.0001, p<0.0001).

Table 1: The demographic and clinical characteristics ofthe study population

Variable	Values
Age (mean years)	35.96
Age (incarl years)	(11.60)
Sex	(11.00)
	14 (53.8%)
Male, n(%)	12 (46.2%)
Female, n(%)	12 (10.270)
Diagnosis Descriptions failure	
Respiratory failure	0
Snakebite envenomation	8
Organophosphate poisoning	8 1
ARDS	1
COPD	2
Fat embolism	1
Acute severe asthma with	1 4
pneumothorax	4
Sepsis	T
Comorbidity (n)	8
Hypertension	2
Diabetes Mellitus	4
Chronic Kidney Disease	1
Hypothyroidism	1
Smoking	9
Insomnia Severity Index (mean)	6.88(2.58)
Epworth Sleepiness Score(mean)	4.92(1.99)
SOFA (mean)	5.1(1.27)
APACHE II (mean)	19.38(3.72)
RASS (median)	0 (-1 - 1)
Ventilator days (mean)	5.38(2.11)
Intensive care unit (ICU) stay in days (mean)	7.38(1.74)

APACHE - Acute Physiology and Chronic Health Evaluation score; SOFA - Severity of Organ Function Assessment score; RASS - Richmond agitation and sedation scale

Table 2. Comparison of PSG data of Intensive Care Units (ICU) and High Dependency Units (HDU) (paired t-test)

	PSG parameters in ICU	PSG parameters in HDU	P-value
TRT	1320.40 (87.76)	1337.31 (65.66)	0.44
SPT	1090.60 (107.85)	1042 (74.22)	0.11
TEST	520.25 (89.59)	499.06 (57.72)	0.25
WASO	579.25 (137.43)	530.73 (98.93)	0.18
N1	148.2 (42.8)	109.36 (25.79)	0.0002
N1%	28.80 (7.30)	21.88 (4.30)	0.0001
N2	315.73 (74.56)	278.71 (38.99)	0.027
N2%	60.3 (8.65)	55.86 (4.00)	0.021
N3	34.19 (12.51)	71.55 (20.53)	<0.0001
N3%	6.66 (2.30)	14.34 (3.87)	<0.0001
REM	22.88 (21.03)	38.44 (19.42)	0.01
REM%	4.20 (3.68)	8.20 (3.54)	0.001
Arousal index	22.65 (10.49)	16.55 (5.15)	0.006
Sleep w/o wake	3.18 (1.35)	4.01 (1.39)	0.03
Day sleep	256.32 (57.33)	188.09 (36.82)	<0.0001
Day sleep %	49.55 (9.29)	37.71 (5.91)	<0.0001
Night sleep	263.72 (68.09)	310.81 (21.02)	0.0016
Night sleep%	50.46 (9.36)	62.28 (8.01)	0.0001

TRT- Total Recording Time; SPT- Sleep Period Time; TST- Total Sleep Time; WASO-Wake Time After Sleep Onset; REM- Rapid Eye Movement

Correlation analysis of variables likely to affect sleep indices

Significant correlation was observed with increasing age and N3% (coeff = 0.539, p= 0.004) and decreased N2% (coeff= -0.431, 0.028). Notably, serum sodium (Na⁺) was weakly associated with the wake up time after sleep onset (coeff= 0.414, p= 0.036) and serum potassium concentration (K⁺) was found to be associated with total sleep time (coeff= 0.467, p= 0.014).

The disease severity (APACHE II) has a weak correlation with the arousal index but failed to reach statistical significance (coeff= 0.347, p= 0.083).

DISCUSSION

The study was conducted in a limited resource setting lacking human resources constraints and technology for routine monitoring of noise, light and sleep promotion strategies in the ICU. Sleep in critically ill patients recovering in intensive care units [3, 6, 12] respectively. Environmental noise was responsible for 11.5 and 17% of the overall arousals and awakenings from sleep, respectively. The mean noise arousal index was 1.9 ± 2.1 arousals/h sleep. Conclusions: (1 and high dependency units [13] is highly disrupted, disturbed, and fragmented. The mean age in the current study represented a

Table 3. Comparison of Illuminance and Sound levels in Intensive Care Units (ICU) and High Dependency Units (HDU) (paired t-test)

	ICU	HINDU	P-value
Light (Illuminance)(Lux)			
Mean illuminance	55.06 (4.68)	112.06 (3.66)	< 0.0001
Mean day illuminance	77.09 (3.66)	160.52 (6.07)	< 0.0001
Mean night illuminance	14.98 (2.04)	23.67(2.62)	< 0.0001
Sound (Noise) level (decibel-dB)- A	-weighted		
Mean sound level	59.17 (1.69)	59.12 (1.49)	0.904
Mean day sound level	62.08 (2.11)	62.07 (2.13)	0.988
Mean night level	53.64 (2.11)	53.67 (1.67)	0.968

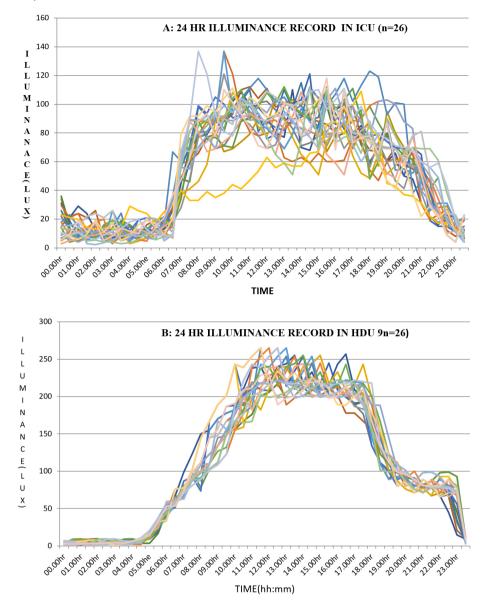


Fig. 2. 24 Hr illuminance records of Intensive Care Units (ICU) (A) and High Dependency Units (HDU) (B) (paired t-test)

younger study group compared to another study [13]. Notably, normal ISI and ESS scores, better pre-hospitalised sleep, and fewer comorbidities observed in the current study may be attributed to the inclusion of a younger age group compared to published literature [13]. The ICU scores reflect the patient's severity of illness and mortality; high ICU scores have severe illness, increased vasopressor use, sedatives, nursing care activities, and ICU stay that can affect sleep quality [1, 3, and 13]. A weak correlation was reported of arousal index (AI) with APACHE II score; notably, Fanfulla et al. (2011) showed a positive correlation of SAPS II with daytime sleepiness in the HDU [13].

Mechanical ventilation, including the mode, has been cited as an important cause of sleep fragmentation and disruption in intensive care units [7, 14, 15]. PSG documented a higher N2 (%) stage and arousal index in the IMV group in the present study. In contrast, the rapid eye movement stage % was recorded more in the spontaneously breathing group. It has been recorded that the ventilatory mode did not influence sleep pattern, arousals, awakenings, and ineffective efforts [13, 15].

All patients being mechanically ventilated received pressure support ventilation, and thus, how different ventilation modes affect sleep architecture could not be analysed.

In the present study, half of the patients received fentanyl 1.g/mL, 1mg, i.v. (NEON, Pharmaceuticals, Mumbai, India) Midazolam (VHB Medicals, Uttara-

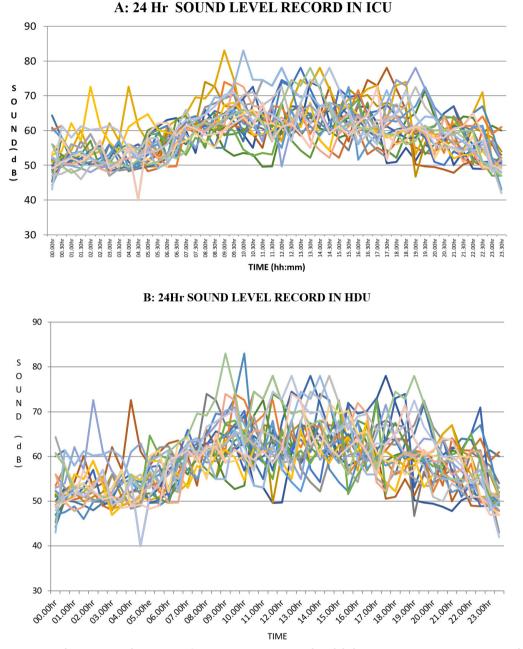


Fig. 3. 24 Hr Sound level (A-weighted) records of Intensive Care Units (ICU) (A) and High Dependency Units (HDU) (B) (paired t-test)

khand, India) the strength, duration, the dosage varied for every patient at every stage according to the clinical conditions.

However, none received benzodiazepines, Propofol, and dexmedetomidine during PSG recordings. In the current study, both PSG indices and patients' perception of sleep using RCSQ were comparable in the opioid and non-opioid groups.

Slow-wave sleep is reduced by opioids, with a concomitant increase in Stage 2 sleep [16]. Elliott et al. (2013) reported increased N2% and total sleep time with decreased Slow-wave sleep and rapid eye movement stage and arousal index (AI) [17]. In another study, patients sedated with Propofol or midazolam infusions reported better sleep quality than non-sedated patients [16]. The differences in the current data and published literature maybe since benzodiazepines and Propofol for sedating patients on PSV were not used during the current study.

Whenever required, patients on mechanical ventilation were given opioids and benzodiazepines 1mg/mL, 25µg, i.v., fentanyl (NEON, Pharmaceuticals, Mumbai, Available online at: www.jccm.ro

India) and 1.g/mL, 1mg, i.v. Midazolam (VHB Medicals, Uttarakhand, India) to maintain comfort during the polysomnography recordings.

Serum potassium levels have been implicated as sleep promotion factors, with hypokalemia causing insomnia and adequate and increasing levels causing sleepiness [18, 19]. Similarly, increasing sodium levels have been linked with difficulty in sleep maintenance [18]. After sleep onset, potassium and sodium levels correlated with total sleep time and wake time in the present study.

Although sleep architecture was poor in both the ICU and HD, patients perceived their sleeplessness to be less disturbed in the HDU compared to the ICU.

When patients recover from critical care illness, changes in the environmental and non-environmental factors such as IMV, drugs, and nursing interactions might be responsible for improving sleep quality.

A light sleep (N1 and N2) stages were predominant, with N3 and REM for only brief periods. This distorted sleep architecture has been consistently reported [5, 12, 17].

On being transferred to the HDU, sleep architecture was different from that in the ICU, with improved N3 (restorative sleep) and REM stage and decreased N1 and N2 proportions. Patients had fewer arousals, and less daytime sleepiness than during their ICU stay.

There is a paucity of data on sleep quality and recovery of sleep disturbances during the critical care illness's early recovery phase. The plausibility of difference in environmental and non-environmental factors in intensive care units and high dependency units and patient-centric factors may contribute to the recovery of sleep architecture.

Kahn et al. (1998) reported a mean sound level of 56/h before a noise reduction program and 40/h afterwards [24]. Freedman et al. (2001) identified that only 11.5% of arousals and 17% of awakenings could be attributed to noise, while Gabor et al. (2003) identified that 20% of awakenings were the direct result of environmental noise [3, 12]. However, Elliott et al. (2013) found no correlation between arousal indices and the number of sound peaks >80 dB [17]. The present study reported no difference in mean sound level in ICU / HDU during daytime and nighttime.

The importance of light as a disruptive factor in an ICU has been postulated and proposed by many studies [26, 27]. Experimental studies showed that an il-

luminance level of 100-500 lux is required to suppress melatonin suppression [26, 28]. In the present study, the intensive care units mean illuminance was < 100 lux. In contrast, the HDU had mean illuminance of

the intensive care units mean illuminance was < 100 lux. In contrast, the HDU had mean illuminance of 160 lux. Consequently, patients in the HDU had lesser daytime somnolence. Consistent findings were also noted by Elliott et al. [17]. The Indian society of critical care medicine (ISCCM) guidelines on ICU design and planning recommend high-intensity natural light in the ICU for better patient outcomes, sleep quality, and decreased delirium incidence and depression [29].

The study was limited by small patient numbers in a single-centre location. The frequent removal of EEG leads during positioning was a typical problem; body movements, nursing care events and positioning made epochs sometimes non-analysable in the R and K systems. Drouot et al. (2012) reported the challenges in scoring ICU patients' sleep data [30]. The interval recording of illuminance and sound level due to instruments' limitations missed the transient increase in illuminance and sound peaks recordings.

The study provides detailed insight into disturbed and fragmented sleep architecture in an ICU and HDU. The sleep disruption showed improvement as the patients were transferred to HDU during recovery. Further research is needed on sleep disruption and recovery in this vulnerable patient population suffering from critical care illness.

AUTHOR CONTRIBUTIONS

Conceptualisation: BP, DC Data curation: BP, DC, ASS, Formal analysis: BP, DC, NG, Methodology: BP, DC. Writing—original draft: BP, DC, Writing—review and editing: BP, DC, ASS, NG.

CONFLICT OF INTEREST

None to declare.

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