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Cognitive impairment in critically ill

KEYWORDS

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Introduction

Survivors of critical illness often suffer from development of new or presumed exacerbation of baseline neurological dysfunctions unrelated to their primary illness.[1,16,17] These events are inadequately characterised and their quantification has been difficult due to limitations imposed by lack of clarity about its epidemiology and pathophysiology. Neurocognitive impairment is increasingly recognized as a prevalent, important, neglected and potentially modifiable outcome among survivors of critically ill patients. It is estimated that close to 5million patients are being managed in an ICU setting annually in the US alone.[2] Data from developing world is not forthcoming. This study was undertaken to study cognitive impairment in critically ill patients admitted to Intensive care unit of a tertiary care hospital. The study aimed to assess prevalence of neurocognitive impairment in critically ill, ascertain the spectrum of neurocognitive impairment in critically ill patients and to determine risk factors associated with development of neurocognitive dysfunction. We also wanted to determine the delayed sequelae of neurocognitive impairment in the critically ill.

Material & Method

Study population and setting

The study was conducted in the medical and surgical ICUs of a tertiary care hospital in Pune, India. At enrolment, written informed consent was obtained from all the participants. The study protocol was approved by the institutional ethics committee.

Study design: Prospective observational study

Study duration & period: 22 months (Aug 2013 to Oct 2015)

Study population: All critically ill patients admitted to the ICU of a tertiary care hospital.

Sample Size: Sample size calculation was not possible as no similar studies were done earlier. Hence this study was planned as a pilot study with sample size of 100.

Inclusion criteria: All adult patients (>18yrs to <70 yrs) with critical illness receiving treatment for respiratory failure and/or shock (cardiogenic or septic) defined as:-

Respiratory failure

A patient was considered to be in respiratory failure if they were receiving invasive mechanical ventilation at the time of enrolment irrespective of the mode of ventilation.

Cardiogenic shock

A patient was considered to be in cardiogenic shock if they were being treated at the time of enrollment with any of the following medications administered for acute cardiac dysfunction: dopamine ≥ 7.5 mcg/kg/min, dobutamine ≥ 5 mcg/kg/min, norepinephrine ≥ 5 mcg/min, phenylephrine ≥ 75 mcg/min, epinephrine at any dose or vasopressin ≥ 0.03 units/min (if used with another vasopressor).

Septic shock

A patient was considered to be in septic shock when suspected or proven infection was documented in the setting of hypotension being treated with any of the previously listed medications.

The following patients were excluded from the study:

– Age < 18years and >75 years
– Substantial recent ICU exposure (defined by 1. Mechanical ventilation in 2months before current ICU stay 2. >72hr with organ dysfunction 3. >5 ICU days in the month preceding current ICU admission)
– Blindness
– Deafness
– Inablility to speak Hindi/ English
– Denied consent
– Difficult to follow up cases- substance abuse, psychotic disorder, residence more than 200km from hospital, unlikely to survive for 24hrs
– Neurodegenerative disease
– Anoxic brain injury
– Severe dementia

Methods

1. 102 consecutive patients admitted to ICU with critical illness meeting the eligibility criteria were enrolled in our study.
2. A thorough physical examination with detailed neurological examination was done.
3. The Short Form Informant Questionnaire On Cognitive Decline in the Elderly (IQCODE) for patients >50 years of age and for patients <50 years but with known memory problems was used to assess any pre-existing neurocognitive impairment.[3]
4. Delirium during hospital stay was assessed using The Confusion Assessment Method for the ICU (CAM-ICU) and Richmond Agitation-SedationScale (RASS). A patient was diagnosed to have delirium if he/ she had a RASS >3 was awake and was CAM-ICU positive.[4,5]
5. The mean ventilation days, use of inotropes and sedatives were noted from the patient's medical records and nursing instruction sheets.
6. Use and duration of physical restraints was examined daily once the patient met eligibility criteria.
7. The data regarding alcohol intake and smoking were obtained from the patient interview and the same confirmed from the primary caregiver.
8. Sedative equivalents were calculated as follows

Table 1: Equivalent dosages of benzodiazepines and opioids

Benzodiazepine equivalent dosage		
Midazolam	Lorazepam	Diazepam
2.5mg	1mg	5mg
Opioid equivalent dosage		
Fentanyl	Morphine	
100mcg	5mg	

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1. The patients were assessed at the time of discharge or at 30 days after weaning off from ventilator by means of a battery of tests which included

a. The components of the PGI-BBD are as follows:

I. PGI Memory Scale (PGIMS)-The PGI memory scale is a part of the PGI brain dysfunction battery developed by Pershad et al., at the PGIMER, Chandigarh in India. It has been validated for use in hindi speaking population. The PGI BBD is a thorough and robust individually administered test designed to assess comprehensively multiple domains of neuropsychological status of adults. The test has been used extensively by various researchers. It has ten sub parts, one each for- remote memory, recent memory, mental balance, attention and concentration (digit span), delayed recall, immediate recall, verbal retention for dissimilar pairs, visual retention, and recognition.[6]

ii. Bender Gestalt test- The Bender Visual Motor Gestalt Test is a psychological test first developed by child neuropsychiatrist Lauretta Bender. The test is employed to evaluate "visual-motor maturity", to screen for developmental disorders, or to assess neurological function or brain damage.[7]

iii. Nahor Benson test- It consists of eight cards. Out of which five cards contain a design each and three cards contain the various instructions to be followed. The subject is asked to copy the designs each of which is based on a developmental pattern. These measure the right hemispheric function especially the parieto-occipital lobe. Scoring is based on all or none principle i.e either correct or incorrect. Each incorrect drawing is given a score of[1].

iv. Trail making test Part B- The Trail Making Test reflects the visuo-conceptual and visuo-motor functions. It is a neuropsychological test of visual attention and task switching.[8,9]

Results

A total of 158 patients were enrolled in the study, 52 died during the admission or before the follow up examination at 3 months and 4 patients were lost to follow up. The study could be completed for 102 patients in total and their outcomes were analyzed.

There were 72 males and 30 females in the study. The mean age was 51.8±13.1 years comprising of 72 Medical ICU and 30 surgical ICU patients.

Prevalence of neuro-cognitive dysfunction

A patient was considered to have neuro-cognitive dysfunction, if he/she was scored positive on any of the psychometric tests positive for dysfunction. The raw scores were calculated and dysfunction scores were derived. Any score other than 0 was considered positive.

At the time of discharge 24.5% patients had neurocognitive impairment. At 3 months of discharge almost 50% of patients had some form of neurocognitive impairment.

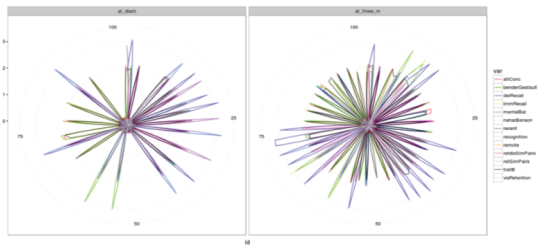
Spectrum of neuro-cognitive dysfunction

1. Delayed recall, recent memory, retention for dissimilar pairs, Bender Gestalt, Nahar Benson and Trail B were predominantly affected. Thus visuomotor and executive functions were primarily impaired and this held true at 3 months also.

2. Attention, immediate recall, mental balance, recent memory, retention for similar pairs, visual retention were far less affected both at the time of discharge and 3 months follow up.

Relationship between the measures

To look for any association between the tests, that is whether a particular test say A and B are detecting similarly as having cognitive dysfunction. The same is depicted by means of a STAR PLOT as given in Chart 1 below.



The star plot depicts the dysfunction scores (0, 2, 3) of each test at discharge and at the end of 3 months on the left and right panel respectively. The spikes are the scores of 2 or 3. We can observe that number of spikes is definitely more at 3 months follow up as compared to that at the time of discharge. There are multiple coloured lines at most of the spikes which tells us that when one test is positive, more number of tests are simultaneously becoming positive. It is also noticed that delayed recall, Bender Gestalt, Nahor Benson and Trail B tests are commonly affected at both the time of discharge and at 3 months followup and that delayed recall is becoming more pronounced at 3 months after discharge.

Risk factors associated with neuro-cognitive derangement

Univariate analysis was used to study the risk factors associated with neurocognitive decline separately at the time of discharge and at 3 months follow up. At the time of discharge, the mean ventilation days, delirium days, presence of respiratory failure, sepsis and alcohol consumption had significant association with development of neurocognitive impairment. The age, sex, use of physical restraints, smoking or the type of ICU admission did not have significant association with development of neurocognitive decline. The Odds ratio and 95% confidence interval are shown in the table 2 below.

Table 2-Risk factors associated with neurocognitive impairment at the time of discharge and 3months follow up

Variable	Levels	At discharge OR (95% CI)	At 03 months OR(95%CI)
Age	Numeric variable per unit increase	1.01(0.97-1.05)	0.99 (0.97-1.03)
Sex	1-2	0.91(0.32-2.41)	1.46 (0.62-3.49)
Mean ventilation days	Numeric variable per unit increase	1.16(1.02-1.40)	1.09 (0.97-1.31)
Educational status	low – high	1.95(0.69-5.30)	1.40 (0.55-3.64)
Sedation	0-No 1-Yes	2.40(0.95-6.09)	1.82 (0.81-4.19)
Physical restraint	0-No 1-Yes	2.33(0.84-6.26)	1.94 (0.77-5.13)
Smoking	0-No 1-Yes	2.25(0.90-5.90)	1.37 (0.63-3.00)
Alcohol	0-No 1-Yes	3.40(1.34-8.83)	1.09(0.48-2.48)
Respiratory failure	0-No 1-Yes	2.64(1.02-7.45)	1.37(0.62-3.02)
Shock	0-No 1-Yes	3.53(1.09-15.88)	2.23(0.92-5.66)
Type of ICU	1-Med ICU 2-Surg ICU	0.91(0.32-2.41)	0.83(0.34-1,94)
Delirium days	Numeric variable per unit increase	2.85(2.02-4.42)	1.50(1.19-1.95)

At 3 months after discharge, the strongest predictor for development of neurocognitive decline was its presence at the time of discharge as all patients who had decline at discharge continued to have it at 3 months. The only other significant factor was the duration of delirium. All the other factors were not significantly associated with neurocognitive decline at 3 months.

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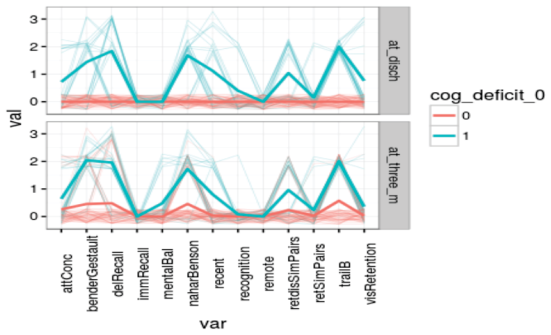
A pictorial representation of the various tests and the degree of derangement is given in Chart 2. From the graph it is obvious that Bender Gestalt, Nahor Benson, delayed recall, retention for dissimilar pairs and Trail B tests were commonly impaired in patients with neurocognitive decline.



Limitations of the study

We acknowledge some limitations of our study design.

1. Our present study included only 102 critically ill patients. The sample size limits the generalizability of our findings, which is a major limitation.

2. Our definition of critically ill patients as having either respiratory failure and/ or shock has not been validated. There may be a risk of misclassification of exposure.

3. Thirdly, as is true for all observational studies, we cannot rule out the possibility that unobserved confounding might have occurred, even after accounting for a number of covariates.

4. The rate of attrition was significant. Attrition is an expected barrier in designing outcomes studies in critical care settings, caused in part by the increased mortality in critically ill patients.

5. The time required for psychometric testing on an average was 90-120 minutes. We expect some of the poor performance may be due to fatigue ensuing out of a long battery of test. Availability of a shorter validated battery could have averted the same.

6. The inclusion of appropriate control groups (i.e., other critically ill patients who did not have ARDS and/or sepsis with matched normal control subjects) needs to be considered in future studies.

7. There are presently no validated tools to quantify severity of delirium, the result of which may have significant impact on the outcome.

Conclusions

Intensivists have traditionally been alerted to dysfunctions in pulmonary, cardiac, and renal parameters as a source of morbidity and mortality in ICU patients. The impact of this illness on brain function has been for long ignored and under-appreciated. These impairments lead to layoffs, absenteeism and rising health care expenditure. There are very few studies on neurocognitive impairment in critically ill patients although physicians world over recognize this as a real yet underreported and understudied issue.[10,11,12]

We found that cognitive impairment can be assessed by administering a battery of tests encompassing multiple domains, but it was challenging and opportunities to improve the performance of this strategy exist. Our findings validate that cognitive morbidity is common in survivors of respiratory failure and sepsis, findings that have significant implications on long-term functioning of these patients. We found evidence that cognitive dysfunction at the time of discharge was the strongest predictor of poor neurocognitive outcome at 3 months.

Although great progress has been made and is ongoing, a pressing need exists for detailed evaluation of cognitive impairment and its many effects, like quality of life, that will seek to untangle the many pertinent questions related to this condition and that will ultimately offer help and hope to the thousands of survivors affected by this condition.[13,14,15] More detailed study with matched controls are required to further our understanding the relative risks and efficacy of preventive interventions on neurocognitive impairment. Risk factors related to the patients and those peculiar to ICU has to be addressed and early interventions initiated to decrease the occurrence of the same. A thorough understanding of mechanisms underlying the development of adverse cognitive outcomes may further our appreciation of its pathophysiology and narrow the knowledge gap that exists currently.[18,19,20,21]

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