

Post ICU syndrome among survivors from respiratory critical illness. A prospective study

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Context Post-ICU syndrome (PICS) is a common impairment that develops after critical illness and persists after discharge. It is considered when a new or worsening impairment in physical, cognitive, or mental status develops among survivors from critical illness.

Aim To assess the prevalence of PICS and to define the profile of patients at risk of each domain.

Patients and methods A total of 420 critically ill patients were assessed at the time of ICU discharge for presence of one or more domains of PICS: cognitive dysfunction, psychiatric impairment, and physical disability.

Results A total of 220 (52.4%) patients without preexisting impairment developed one or more PICS forms. Half of the participants developed cognitive impairment, 14.29% developed depression, 26.19 developed anxiety, and 35.71% experienced both muscle weakness and impaired balance. PICS presented in three different patterns: pattern A, with one domain, in which 2.38% presented with either cognitive or psychiatric affection; pattern B, with two (19.05%) domains, where 80 patients had cognitive dysfunction, combined with physical affection in 30 patients and psychiatric impairment in 50 patients; and pattern C, with all PICS domains (28.57%).

Introduction

Post-ICU syndrome (PICS) is a common impairment that develops after critical illness and persists after discharge from ICU. It is considered when a new or worsening impairment in physical, cognitive, or mental health status develops among survivors from critical illness [1].

Long-term cognitive impairment is reported to occur in 25% of ICU survivors, a percent that reaches 75% in a few studies [2]. Risk factors include prior cognitive impairment, prolonged mechanical ventilation (MV), glucose dysregulation, duration of delirium, stroke, alcoholism, hypoxia, hypotension, severe sepsis, and acute respiratory distress syndrome (ARDS) [3].

Moreover, psychological disability (anxiety, depression, and posttraumatic stress disorder) is observed up to 62% among survivors after discharge from ICU with the same risk factors for cognitive dysfunction in addition to the use of sedation and analgesia in ICU, female sex, lower level of education, and preexisting psychiatric impairment [4–6].

Critical illness neuromuscular weakness is considered the most common physical impairment that occurs in

Multivariate analysis was used to detect independent predictors associated with each domain of PICS.

Conclusion Survivors from critical illness should be screened for different domains of PICS. Cognitive impairment was evident in those with prolonged duration of mechanical ventilation (MV), delirium, stroke, and hypotension. Psychiatric impairment was evident in females with prolonged sedation and duration of MV, delirium, and hypoglycemia. Physical impairments were evident in those with sepsis, undernutrition, and prolonged duration of MV.

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more than quarter of ICU population. Risks include multisystem organ failure, sepsis, prolonged sedation use, and MV (>7 days) [7,8].

This study aimed at assessment of the prevalence of PICS among survivors from respiratory critical illness and to define the profile of patients at risk of each domain.

Patients and methods

This study was conducted at respiratory ICU (RICU), Zagazig University Hospitals, from January 2017 to January 2019. It included 420 critically ill patients assessed at time of ICU discharge.

Inclusion criteria

All critically ill patients admitted to RICU for more than 24 h owing to various diagnoses with no history of neurocognitive impairment during the period of the study and who agreed to participate were included.

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Exclusion criteria

Participants with any of the followings were excluded: malignancy, neuromuscular pathology, pregnancy, and patients discharged on long-term ventilatory support or tracheostomy.

All participants were subjected to the followings:

- (1) Good history taking and event documentation during RICU stay with stress on previous ICU admission or MV, respiratory failure, recent ventilatory support and its duration, sepsis, use of sedation, cardiac arrest, ARDS, stroke, delirium, undernutrition, hypoglycemia, hypotension, and hypoxemia.
- (2) Assessment of cognitive impairment using Montreal Cognitive Assessment scale, Arabic version. It is a 30-point test in which a score less than 26 points represents a mild cognitive affection [9].
- (3) Assessment of psychosocial problems:
 - (a) The Generalized Anxiety Disorder-7 scale, Arabic version: scores of 5, 10, and 15 are the cut-off points for mild, moderate, and severe anxiety, respectively [10].
 - (b) Beck Depression Inventory-second edition scale, the Arabic translation: it assesses the presence and severity of depression. Each item is related to how the patient had felt in the previous two weeks. There is a four-point scale for each item ranging from 0 to 3. Total score of 14–19 represents mild form of depression, 20–28 represents moderate form, and 29–63 represents severe form [11].
- (4) Assessment of muscle power strength using Medical Research Council sum score: the sum of the manual muscle test using the Oxford 0–5 scales for the following muscle groups bilaterally – shoulder abduction, elbow flexion, wrist extension, hip flexion, knee extension, and dorsiflexion. A score of less than 48/ is consistent with ICU-acquired weakness [12].
- (5) Balance evaluation using Berg Balance Scale. Score of less than 45/58 indicates an increased risk for falls [13].

Ethical statement

The study was approved by Ethics Committee of Faculty of Medicine, Zagazig University. A written informed consent was obtained from all participants.

Statistical analysis

All statistics were performed using Minitab 17.1.0.0 for Windows (2013; Minitab Inc., State College, PA,

USA). Continuous variables were presented as mean (SD) and nonparametric data as number (%). Multivariate logistic regression analysis with stepwise elimination was used to determinate the independent predictors of PICS domains. *P* value above 0.05 was considered significant.

Results

This study enrolled 695 patients; of them, 420 patients completed the study, as 75 patients were excluded according to the exclusion criteria, 80 patients died before discharge, and 95 patients refused to participate. A total of 420 survivors from critical illness were evaluated at the time of ICU discharge. Table 1 demonstrated the prevalence of different domains of PICS. Overall, 220 (52.4%) patients without preexisting impairment developed one or more PICS forms. Half of the participants developed cognitive impairment, 14.29% developed depression, 26.19% developed anxiety, and finally, 35.71% experienced both muscle weakness and impaired balance.

Different patterns of PICS were shown in Table 2. PICS presented in three different patterns: pattern A, with one domain, in which 2.3% presented with either cognitive or psychiatric affection; pattern B, with two

Table 1 Prevalence of different domains of post-intensive care unit syndrome

Post-ICU syndrome domain	Total (N=420)	
Cognitive dysfunction	210	50
Depression	60	14.29
Anxiety	110	26.19
Muscle weakness	150	35.71
Balance affection	150	35.71

Categorical data represented as *n* (%).

Table 2 Patterns of post-intensive care unit syndrome

Post-ICU syndrome patterns	Total (N=420)	
Free	200	47.62
A pattern	20	4.76
Cognitive dysfunction	10	2.38
Physical disorder	10	2.38
B pattern	80	19.05
Cognitive dysfunction	80	19.05
Physical disorder	30	7.14
Psychic disorder	50	11.90
C pattern	120	28.57
Cognitive dysfunction	120	28.57
Physical disorder	120	28.57
Psychic disorder	120	28.57

Categorical data represented as *n* (%). A pattern, patients with one form of post-ICU disorders; B pattern, patients with two forms of post-ICU disorders; C pattern, patients with all forms of post-ICU disorders.

(19.05%) domains, where 80 patients had cognitive dysfunction, combined with physical affection in 30 patients and psychiatric impairment in 50 patients; and pattern C, with all PICS domains (28.57%).

Demographic and risk factors of patients with PICS are shown in Table 3. In this study, patients at risk of PICS had mean age of 51.23±10.07 years, 65% were males, previously ICU admitted were 31.82%, and previously mechanically ventilated were 9.09%. Recent institution of ventilatory support owing to respiratory failure was observed in 95.45%, with mean duration of MV of 9.82±4.21 days. Sepsis was found in 13.64%, prolonged sedation in 36.36%, cardiac arrest in 4.55%, ARDS in 13.64%, stroke in 18.18%, delirium in 45.45%, poor nutrition in 45.45%, hypoglycemia in 18.18%, and finally hypotension in 22.73%.

Multiple regression analysis of variables associated with each domain of PICS is shown in Tables 4–6. Multiple regression analysis of variables associated with post-ICU cognitive dysfunction revealed four independent predictors: duration of MV [odds ratio (OR)=1.19, confidence interval (CI)=1.1–1.28, $P<0.001$], stroke (OR=2.52, CI=0.95–6.69, $P=0.038$), delirium (OR=3.21, CI=1.76–5.84, $P<0.001$), and hypotension (OR=3.44, CI=1.52–7.67, $P=0.002$). Multiple regression analysis of variables associated with post-ICU psychiatric disorder revealed five independent predictors: duration of MV (OR=0.80, CI=0.669–0.946, $P=0.005$), prolonged use of sedation (OR=11.50, CI=24.55–52.64, $P<0.001$),

delirium (OR=4.92, CI=2.094–11.55, $P<0.001$), hypoglycemia (OR=9.96, CI=3.068–32.31, $P=0.02$), and female sex (OR=0.01, CI=0.005–0.0349, $P=0.01$). Multiple regression analysis of variables associated with post-ICU physical disorder revealed three independent risk factors: duration of MV (OR=1.35, CI=1.2073–1.517, $P<0.001$), undernutrition (OR=0.88, CI=0.393–1.963, $P=0.015$), and sepsis (OR=6.28, CI=1.323–29.801, $P=0.02$).

Discussion

In the current study, among 420 survivors enrolled and assessed at the time of discharge from ICU, 200 (47.6%) patients were free from PICS, whereas 220

Table 3 Demography and risk factors of patients with post-intensive care unit syndrome

Characteristics	Total (N=220)	
Age	51.23	10.07
Sex (male)	143	65
Previous ICU admission (yes)	70	31.82
Previous MV	20	9.09
Recent MV	210	95.45
Duration of MV use	9.82	4.21
Sepsis	30	13.64
Prolonged sedation	80	36.36
Respiratory failure	210	95.45
Cardiac arrest	10	4.55
ARDS	30	13.64
Stroke	40	18.18
Delirium	100	45.45
Undernutrition	100	45.45
Hypoglycemia	40	18.18
Hypotension	50	22.73
Hypoxemia	210	95.45

ARDS, acute respiratory distress syndrome; MV, mechanical ventilation. Continuous data were represented as mean and SD, categorical data as n (%).

Table 4 Multiple regression analysis of variables associated with post-intensive care unit cognitive dysfunction

Factors	OR	95% CI	P
Age	0.99	(0.9656, 1.0167)	0.48
Duration of MV use	1.19	(1.1019, 1.2887)	<0.001
Stroke	2.52	(0.9504, 6.6978)	0.038
Delirium	3.21	(1.7657, 5.8448)	<0.001
Hypoglycemia	3.55	(1.4006, 8.9820)	0.07
Hypotension (septic shock)	3.44	(1.5205, 7.7645)	0.002

Pearson; $\chi^2=404.6$, $P=0.5$, the model was adjusted for all variables using stepwise elimination. CI, confidence interval; MV, mechanical ventilation; OR, odds ratio. P value considered significant if less than 0.05.

Table 5 Multiple regression analysis of variables associated with post-intensive care unit psychiatric disorder

Factors	OR	95% CI	P
Duration of MV use	0.80	(0.6696, 0.9465)	0.005
Prolonged sedation	11.50	(24.5536, 52.6416)	<0.001
Delirium	4.92	(2.0949, 11.5522)	<0.001
Hypoglycemia	9.96	(3.0686, 32.3122)	0.02
Sex (female)	0.01	(0.0051, 0.0349)	0.01

Pearson; $\chi^2=203.4$, $P=1$, the model was adjusted for all variables using stepwise elimination. CI, confidence interval; MV, mechanical ventilation; OR, odds ratio. P value considered significant if less than 0.05.

Table 6 Multiple regression analysis of variables associated with post-intensive care unit physical disorder

Factors	OR	95% CI	P
Age	0.97	(0.9367, 0.9946)	0.2
Previous ICU admission	2.22	(0.9760, 5.0288)	0.06
Previous MV support	3.44	(0.4460, 26.6083)	0.23
Duration of MV use	1.35	(1.2073, 1.5175)	<0.001
Undernutrition	0.88	(0.3932, 1.9639)	0.015
Sepsis	6.28	(1.3238, 29.8016)	0.02

Deviance; $\chi^2=258.7$, $P=1$, the model was adjusted for all variables using stepwise elimination. CI, confidence interval; MV, mechanical ventilation; OR, odds ratio. P value considered significant if less than 0.05.

(52.4%) patients without preexisting impairment developed one or more PICS forms.

Half of the participants developed post-ICU cognitive impairment, 14.29% developed depression, 26.19% developed anxiety, and finally 35.71% experienced both ICU muscle weakness and impaired balance.

In a study by Marra *et al.* [14], one or more PICS problems were present in 64% and 56% after 3 months and 1 year after discharge, respectively. Of patients assessed, 38% had cognitive dysfunction, 26% had physical weakness, and 33% had depressive impairment. At 12 months, 33% had cognitive impairment, 21% had disability, and 31% had depression.

One study reviewed the medical records of patients referred for psychiatric consultation and screening of cognitive dysfunction or mood affection at discharge from the ICU during the 12-month period, and 43.3% screened positive for cognitive impairment and 60% experienced depressive symptoms [15].

Jones *et al.* [16] reported that 86.7% of patients one week after discharge from ICU showed evidence of strategic thinking and problem-solving impairment.

In Torgersen *et al.* [17], 64.3% of enrolled patients had a cognitive impairment at time of ICU discharge.

Global cognition and executive function were assessed in the study by Pandharipande *et al.* [18] 3 and 12 months after discharge on 821 adults with respiratory failure or shock. Overall, 6% of their participants had cognitive impairment at baseline. After 3 months, 40% of participants had cognitive score similar to patients with moderate traumatic brain injury (1.5 SD), and 26% had scores similar to patients with mild Alzheimer's disease (2 SD).

In the current study, PICS presented in three different patterns: pattern A, which had one domain, in which 2.3% presented with either cognitive or psychiatric affection; pattern B, with two domains (19.05%), where 80 patients had all cognitive dysfunction combined with physical affection in 30 patients and psychiatric impairment in 50 patients; and pattern C, which developed all PICS domains (28.57%).

Marra *et al.* [14] reported that co-occurrence of two or more PICS domains was present in 25% of patients at 3 months and 21% of them after 1 year of discharge. All domains of PICS were present in only 6 and 4% at 3 and 12 months, respectively.

In this study, patients at risk of PICS had mean age of 51.23 ± 10.07 years, 65% were males, previously ICU admitted patients represented 31.82%, and previously mechanically ventilated patients represented 9.09%. Recent institution of ventilatory support owing to respiratory failure was observed in 95.45%, with mean duration of MV of 9.82 ± 4.21 days. Sepsis was found in 13.64%, prolonged sedation in 36.36%, cardiac arrest in 4.55%, ARDS in 13.64%, stroke in 18.18%, delirium in 45.45%, poor nutrition in 45.45%, hypoglycemia in 18.18%, and finally hypotension in 22.73%.

Marra *et al.* [14] found that survivors who were free from PICS tended to be younger, more educated, less frail, and had fewer comorbidities than those with PICS. Severity of illness on admission was similar between those with or without PICS. Patients who were mechanically ventilated, developed sepsis, coma, or delirium during ICU course were more likely to have PICS.

In comparison with studies that assessed PICS in general ICUS, our results agreed that more than five of every 10 patients developed PICS and the majority developed cognitive impairment. On the contrary, in general ICU, the majority developed one domain of PICS and was suggested to be a sequela of severe critical illness rather than part of syndrome, whereas in the current work, more than one in every four patients developed PICS with all three domains. This difference can be attributable to the following: first, different patient characteristics in RICU, in which 95% of the studied population had respiratory failure and blood gases disturbances in addition to share a high percent of other accusing factors of PICS with general ICUS, and second, the different enrolling criteria and PICS definition between studies. In this study, only new insults were taken into consideration, and patients were included on the basis of not having a previous defect compared with other studies that included those with new or worsened previous dysfunction [1,5,7].

Multiple regression analysis of variables associated with post-ICU cognitive dysfunction revealed four independent predictors: duration of MV, stroke, delirium, hypotension (Table 4). Chung *et al.* [15] in their study pointed contrary results, in which post-ICU cognitive impairment was not associated with the usual risk factors including age, preexisting cognitive impairment, and duration of delirium in the ICU but was associated with the initial severity of illness assessed by SOFA score.

Pandharipande *et al.* [18] concluded that persistent worsened cognition was independently associated with longer duration of delirium, a finding that was not influenced by sedation or analgesia, age, preexisting cognition, and organ failures during ICU course.

Multiple regression analysis of variables associated with post-ICU psychiatric disorder revealed five independent predictors: duration of MV, prolonged use of sedation, delirium, hypoglycemia, and female sex (Table 5).

Chung *et al.* [15] in their report found a significant association between female sex (88.9%) and post-critical illness depressive disability and trends of association between post-ICU memories and duration of ventilatory support and ICU length of stay.

Davydow *et al.* [19] in their systematic review included 1213 patients and reported a prevalence of post-critical illness significant depression in 28%. Neither sex nor age was an independent risk factor. Moreover, severity of illness on admission was not a risk factor. However, early post-ICU depressive symptoms were a strong predictor for subsequent depression.

Multiple regression analysis of variables associated with post-ICU physical disorder revealed three independent risk factors: duration of MV, undernutrition, and sepsis (Table 6).

Regarding study limitation, this study assessed short-term acute effects of surviving a critical care illness as all evaluation was done at the time of discharge, but long-term effects that might persist cannot be assessed owing to difficult follow-up and recruitment of survivors in multiple assessment visits.

Conclusion

Survivors from critical illness should be screened for different domains of PICS. Half of participants in the current work experienced post-ICU cognitive impairment, which was evident in those with prolonged duration of MV, delirium, stroke, and hypotension. Moreover, 14.29 and 26.19% were reported to have depression and anxiety, respectively, which were more evident in females with prolonged duration of MV and sedation, delirium, and hypoglycemia. Finally, post-ICU physical impairments were reported in 35.71%, which was evident in those with sepsis, undernutrition, and prolonged duration of MV.

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Conflicts of interest

There are no conflicts of interest.

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