



ORIGINAL ARTICLE

## Frequency and spectrum of Post-Intensive Care Syndrome (PICS) in survivors of critical illness in a tertiary care hospital in Pakistan.

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**ABSTRACT... Objective:** To determine the frequency and spectrum of post-intensive care syndrome (PICS) in survivors of critical illness at a tertiary care hospital of Pakistan. **Study Design:** Cross-sectional study. **Setting:** Intensive Care Unit (ICU) of the Sindh Institute of Urology and Transplantation, Karachi, Pakistan. **Period:** November 2022 to July 2023. **Methods:** Critical illness survivors aged 18-75 years and discharged from intensive care units ICUs were analyzed. PICS was defined as new or worsening problem(s) in physical, cognitive, or mental health status arising after critical illness and persisting beyond acute care hospitalization. Montreal Cognitive Assessment (MoCA), Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder-7 (GAD-7), and Clinical Frailty Scale (CFS) were used to evaluate cognitive, psychiatric, and physical impairments. **Results:** There were 91 patients, with a median age of 40 years (IQR = 23 - 48). Physical impairment was observed in 49.4% of patients, whereas cognitive impairment was found in 67%, and psychiatric impairment (based on PHQ-9 scores of 5 or greater and GAD-7 scores of 5 or greater) was observed in 49.4% and 45.0% of patients, respectively. Overall, the frequency of PICS was found to be 84.6% in our study, and the frequency of patients with impairment in 1, 2, or 3 domains was 33%, 14.3%, and 37.4%, respectively. **Conclusion:** PICS is a highly prevalent syndrome in survivors of critical illness. Shock is a statistically significant risk factor for PICS. Cognitive impairment appears to be the most common domain of PICS.

**Key words:** Critical Illness, Cognitive Impairment, Intensive Care Unit, Post-intensive Care Syndrome, Shock.

### INTRODUCTION

Post-Intensive Care Syndrome (PICS) is a new or worsening problem(s) in physical, cognitive, or mental health status arising after a critical illness and persisting beyond acute care hospitalization.<sup>1</sup> Overall, the incidence of PICS is around 50%, but the incidence of cognitive, psychiatric, and physical impairments may be as high as 78%, 62%, and 64%, respectively, in survivors of critical illness.<sup>2-5</sup> In addition to these three inter-related domains of PICS, there are many other significant health problems that frequently and adversely affect critical illness survivors like fatigue, malnutrition, reduced lung function, poor sleep, and an inability to adapt to social roles.<sup>5</sup>

The Society of Critical Care Medicine (SCCM) has recently reaffirmed the core domains of PICS, including physical, cognitive, and mental health,

along with social health/return to social roles. In addition, SCCM has strongly recommended identifying PICS proactively and seeking proactive guidance in managing different and broad-ranging domains of PICS.<sup>6</sup> Thus, with an ever-increasing population of survivors of critical illness, especially those with risk factors for PICS, it is imperative to look after them, with standard and recommended tools holistically. Post-discharge care of survivors of critical illness is sub-optimal, as there are neither dedicated clinics nor specified doctors. During this immediate post-discharge period, suffer from increased vulnerability to further deterioration, repeated hospitalization(s), and even death. Despite its high frequency, there is no healthcare facility/department to diagnose PICS. Thus, identifying PICS is the first step that may lead to proper management of PICS by the relevant healthcare teams. The purpose of the

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study was to determine the frequency and the spectrum of PICS in critical illness survivors.

## METHODS

This was a cross-sectional study conducted in ICUs of the Sindh Institute of Urology and Transplantation, Karachi, Pakistan, from November 2022 to July 2023. The sample size of 91 was calculated using open epi software based on the anticipated frequency of psychiatric impairment as 62%<sup>4</sup>, with a margin of error of 10% and 95% confidence level. We used purposive consecutive sampling technique. Approval from Ethical Review Committee (SIUT-ERC-2023/A-425) (Dated January 2, 2023) was obtained. Inclusion criteria were critical illness survivors aged 18-65 years, stayed and discharged from ICU after a minimum period of 24 hours. Patients unwilling to be part of the study were excluded. Informed and written consents were obtained from all study cases. PICS was defined as a new or worsening impairment in the physical, cognitive, or psychiatric domain. Impairment in any one of these domains was considered as PICS.<sup>7</sup> Survivors of critical illness were defined as patients who required intensive care unit admission for a period above 24 hours and were discharged home. Cognitive impairment was labeled if the MoCA score was less than 26. Depression was identified by Patient Health Questionnaire-9 (PHQ-9) with scores above 4.<sup>8</sup> Anxiety was identified using Generalized Anxiety disorder-7 (GAD-7) scores above 4.<sup>9,10</sup> Physical disability was labeled if Clinical Frailty Scale (CFS) score was above 4.<sup>11</sup>

We contacted the patient using the available phone number in the electronic database and took verbal consent after explaining the objectives of our research. A visit of the enrolled patient was scheduled on the date and time of his/her convenience. The researchers physically examined and interviewed the participants of the study. The comprehensive proforma, including the GAD-7, PHQ-9, and MoCA questionnaires, were filled out as per the information provided by the participants.

All the data was secured and entered into IBM-SPSS Statistics, version 26.0. Normality

distributed of continuous variables like age, scores of MoCA, PHQ-9, and GAD-7 were checked and represented as mean and standard deviation or median and inter-quartile range (IQR). Categorical variables such as gender, CFS, education level, risk factors, and comorbidities were presented as frequencies and percentages. A p-value of < 0.05 was considered statistically significant.

## RESULTS

In a total of 91 patients, the median age was 40 years (23-48). There were 58 (63.7%) patients who were male. Hypertension was the most frequent comorbidity, noted in 34 (37.4) patients. Overall, the frequency of PICS was found to be 77 (84.6%). Table-I is showing comparison of demographics and clinical characteristics of survivors with respect to critical illness.

The mean length of ICU stay was  $4.88 \pm 6.61$  days, whereas the mean length of hospital stay was  $11.49 \pm 8.33$  days. The frequencies of pre-existing mental health problems and pre-existing frailty were 14.2% and 13.1%, respectively (Table-II).

The median pre- and post-morbid CFS were 3 (IQR=3.0-4.0) and 4 (IQR=4.0-5.0) respectively. Physical impairment, in the form of CFS>4 was observed in 49.4% of patients, whereas cognitive impairment (MoCA <26) was found in 67%, and psychiatric impairment (based on PHQ-9  $\geq$  5 and GAD-7  $\geq$  5) was observed in 49.4% and 45.0% of the patients. In our study, and the frequency of patients with 1,2 or 3 domains was 33.0%, 14.3%, and 37.4%, respectively (Table-III).

## DISCUSSION

Our study showed a higher frequency of e PICS when compared to others.<sup>2</sup> This may genuinely relate to patients' conditions or slow recovery, but it may also be due to several other factors, such as earlier timing of the follow-up (within the first month versus later), a lack of formal education in most of our study population, and previously under-recognized impairments that became apparent immediately after discharge from the ICU. In a recent study<sup>12</sup>, the highest incidence of PICS was 64% at a 1-year follow-up.

Characteristics		Total n (%)	PICS Present n (%)	PICS Absent n (%)	P-Value
Ag (years)	18-40	45 (49.4)	35 (38.4)	10 (10.9)	0.074
	41-65	46 (50.5)	42 (46.1)	4 (4.3)	
Gender	Males	58 (63.7)	46 (50.5)	12 (13.1)	0.063
	Females	33 (36.3)	31 (34.0)	2 (2.1)	
Marital Status	Married	59 (64.8)	57 (62.6)	2 (2.1)	<0.001
	Never married	22 (24.2)	14 (15.3)	8 (8.7)	
	Previously married	10 (11.0)	6 (6.5)	4 (4.3)	
Education	None	39 (42.9)	29 (31.8)	10 (10.9)	0.033
	Primary	16 (17.6)	16 (17.5)	-	
	Matriculation	14 (15.4)	14 (15.3)	-	
	Graduation or higher	22 (24.2)	18 (19.7)	4 (5.4)	
Pre-morbid employment status	Employed	38 (41.8)	30 (32.9)	8 (8.7)	0.204
	Unemployed	53 (58.2)	47 (51.6)	4 (4.3)	
Post-morbid employment status	Employed	20 (22.0)	14 (15.5)	6 (6.5)	0.073
	Unemployed	71 (78)	63 (69.2)	8 (8.7)	
Co-Morbidities	Diabetes	15 (16.5)	15 (16.4)	0 (0)	0.115
	Hypertension	34 (37.4)	32 (35.1)	2 (2.1)	0.052
	Heart disease	6 (6.6)	6 (6.5)	-	0.585
	Lung Disease	6 (6.6)	6 (6.5)	-	0.585
	Arthritis	10 (11.0)	10 (10.9)	-	0.351
	Renal disease (excluding dialysis)	26 (28.6)	24 (26.3)	2 (2.1)	0.335
	On Hemodialysis	16 (17.6)	14 (15.3)	2 (2.1)	1.000

**Table-I. Demographics and clinical characteristics of survivors of critical illness (N=139)**

Variables		Total n (%)	PICS Present n (%)	PICS Absent n (%)	P-Value
Mean length of ICU stay in days (SD)		4.88 (6.61)	5.06 (7.02)	3.86 (3.57)	0.290
Mean length of hospital stay in days (SD)		11.49 (8.33)	11.84 (8.85)	9.57 (4.25)	0.458
Pre-existing mental health problems		13 (14.2)	13 (14.2)	-	0.206
Adequate social support		20 (21.9)	16 (17.5)	4 (4.3)	0.499
Pre-existing frailty		12 (13.1)	10 (10.9)	2 (2.1)	1.000
Pre-morbid CFS	CFS 2	36 (39.6)	30 (32.9)	6 (6.5)	0.675
	CFS 3	19 (20.9)	15 (16.4)	4 (4.3)	
	CFS 4	26 (28.6)	22 (24.1)	4 (4.3)	
	CFS 5	8 (8.8)	8 (8.7)	-	
	CFS 6	2 (2.2)	2 (2.1)	-	
Post-morbid CFS	CFS 2	8 (8.8)	2 (2.1)	6 (6.5)	<0.001
	CFS 3	6 (6.6)	4 (4.3)	2 (2.1)	
	CFS 4	32 (35.2)	30 (32.9)	2 (2.1)	
	CFS 5	24 (26.4)	20 (21.9)	4 (4.3)	
	CFS 6	19 (20.9)	19 (20.8)	-	
	CFS 7	2 (2.2)	2 (2.1)	-	
MoCA score	< 26	61 (67.0)	-	-	0.002
	≥26	30 (33.0)	20 (21.9)	10 (10.9)	
PHQ-9 Score (depression)	Less than 5	46 (50.6)	33 (36.2)	14 (15.3)	<0.001
	5 or more	45 (49.4)	43 (47.2)	-	
GAD-7 score (anxiety)	Less than 5	50 (55)	36 (39.5)	14 (15.3)	<0.001
	5 or more	41 (45)	41 (45.0)	-	

**Table-II. Comparison of outcome variables respect to presence of PICS (N=139)**

SD: standard deviation, CFS: clinical frailty score, IQR: Interquartile range  
 MoCA: Montreal Cognitive Assessment, PHQ: Patient Health Questionnaire  
 GAD: Generalised Anxiety Disorder Assessment, PICS: post intensive care syndrome

Domain	Risk Factor	PICS Present	PICS Absent	P-Value
For Cognitive Impairment				
Sepsis	Present	61 (67.0)	10 (10.9)	0.499
	Absent	16 (17.5)	4 (4.3)	
Respiratory Failure	present	55 (60.4)	10 (10.9)	1.000
	absent	22 (24.1)	4 (4.3)	
Shock	present	25 (18.6)	-	0.009
	absent	52 (57.1)	14 (15.3)	
Mechanical ventilation	Yes	37 (40.6)	6 (6.5)	0.720
	No	40 (43.9)	8 (8.7)	
For Psychiatric Impairment				
Pre-existing mental health problems	Yes	13 (14.2)	0 (0)	0.099
	No	64 (70.3)	14 (15.3)	
Adequate social support	Yes	61 (67.0)	10 (10.9)	0.499
	No	16 (17.5)	4 (4.3)	
For Physical Impairment				
Pre-morbid frailty	Yes	10 (10.9)	2 (2.1)	1.000
	No	67 (73.6)	12 (13.1)	

**Table-III. Association of risk factors with PICS**

PICS: post intensive care syndrome

The early follow-up may have contributed to a higher incidence in our study. Calculating the incidence of PICS is inherently difficult due to the unknown premorbid status of the patients and the inevitable reliance on recalling patients' baseline functional status by the patients or their attendants. Although the "Society of Critical Care Medicine (SCCM)" has recommended a timeframe of 2-4 weeks for the evaluation of PICS, many studies have evaluated long-term outcomes, about 6 to 12 months after discharge from the ICU.

Education appears to be a significant contributing factor to PICS, and higher education seems to lower the likelihood of PICS.<sup>12</sup> We could not evaluate all risk factors of PICS in our study population, as factors like delirium, APACHE scores (or other severity of illness scores), and sedation with benzodiazepines versus other drugs<sup>13</sup> are not routinely documented. However, we found shock to be a statistically significant risk factor for PICS. Shock is significantly associated with cognitive impairment<sup>2</sup>, although a recent study found no association.<sup>13</sup> Although hypertension was found to be the most common comorbidity, it did not reach statistical significance for PICS. A larger sample size might confirm the association between hypertension and PICS.

About 50% of the study population were frail with a CFS score of 5 or higher after discharge from the hospital.<sup>14-16</sup> It is higher than other studies: Bagshaw et al the reason may be the higher premorbid CFS (median CFS =3).<sup>6</sup> The CFS scoring was based on a CFS classification tree that adds to the validity of our CFS scoring.<sup>17</sup>

When discussing PICS, "Montreal Cognitive Assessment (MOCA)" score of less than 26 and "Patient Health Questionnaire-9 (PHQ-9)" and "Generalized Anxiety Disorder-7 (GAD-7)" scores of 5 or more were considered indicative of PICS. As MOCA could not be assessed before the illness for obvious reasons, and objective assessments of depression and anxiety were also not possible premorbid, it is uncertain whether this was a new finding. This may have contributed to the higher prevalence of PICS in our population. Frailty is assessed by the CFS as it encompasses the functionality of the patient as a person, and not just individual organ function. PHQ-9 and GAD-7 were used as their validated translations in the Urdu language were available.<sup>12,14</sup>

Post-intensive care syndrome is a prevalent but under-recognized problem in developing countries, and there was a need to study this subject in our population. The follow-up after

discharge from the hospital is usually done by non-ICU physicians who may not be aware of the full spectrum of PICS, its risk factors, and optimal management. We conducted this study to highlight the high frequency of PICS in our population.

This is the first study to address PICS in our population, designed based on validated scales and data obtained within the stipulated time frame of one month post-discharge from the hospital. There are a few limitations in our study, including the lack of education among the participants. The premorbid status of the patients was evaluated subjectively and could not be validated. For this reason, there was a chance of miscalculating the frequency of new impairments in our study population.

## CONCLUSION

PICS is a highly prevalent syndrome in survivors of critical illness. Shock is a statistically significant risk factor for PICS. Cognitive impairment appears to be the most common domain of PICS.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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
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2	Fakhir Raza Haidri	Concept and Designing, Proof reading, Critical revisions.	
3	Mujtaba Hassan	Concept and Designing, Proof reading, Critical revisions.	
4	Syeda Shaheera Zaidi	Literature review, Data analysis, Discussion.	