

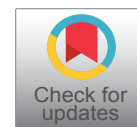


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## OBSERVATIONAL STUDY

# A Case Control Study of Risk Factors for Depression in Intensive Care Unit Patients

**Sherif Abdelmonem, PhD<sup>1</sup>, Ghada Abdel Hadi, PhD<sup>2</sup>, Akram Fayed, PhD<sup>1</sup>, Iman El Sayed, PhD<sup>3\*</sup> and Khaled Mogazy, MSc<sup>1</sup>**



<sup>1</sup>Department of Critical Care Medicine, Faculty of Medicine, Alexandria University, Egypt

<sup>2</sup>Department of Neurology and Psychiatry, Faculty of Medicine, Alexandria University, Egypt

<sup>3</sup>Department of Biomedical Informatics and Medical Statistics, Medical Research Institute, Alexandria University, Egypt

**\*Corresponding author:** Iman El Sayed, PhD, Department of Biomedical Informatics and Medical Statistics, Medical Research Institute, Alexandria University, 165<sup>th</sup> El Hureya avenue, Alexandria, Egypt, Tel: +20116631103, Fax: +2034285455

## Abstract

**Background:** We aim to detect the prevalence and risk factors of depression in Intensive Care Unit (ICU) patients.

**Methods:** A case-control study was conducted on 159 adult patients admitted to the ICU of a governmental hospital, Alexandria, Egypt. We classified the patients using the Arabic version of Hamilton scale as either depressed or not. Bivariate and multivariate analyses were done to detect the relation between depression and different predictors after controlling the confounding effect of all other factors.

**Results:** The prevalence of depression in the ICU patients was 46.5%. The strongest risk factor for depression was female gender (Odds ratio (OR) 46.4, 95% CI: 11.3 to 189.9). One-year increase in age increases the odds of depression by 5% (OR 1.05, 95% CI: 1.01 to 1.09). The odds of depression increased 22 times more in mechanically ventilated patients (OR 22.95% CI: 4.78 to 101.85). The OR of depression was 4.39 (95% CI: 1.29 to 14.97) among patients with cardiac arrest history.

**Conclusion:** The high prevalence of depression among ICU patients requires attention especially among old female patients, those on mechanical ventilation and those with previous cardiac arrest history.

## Keywords

Depression, Case-control studies, Risk factors, Heart arrest, Intensive care unit, Female

## "What this paper adds"

### 1. What is already known on this subject:

- Critical illnesses and Intensive Care Unit (ICU) therapies expose patients to extreme stressors.
- Clinicians are interested in discovering more about these psycho-social outcomes and intervening to improve them.
- A clinical guideline from the British National Institute of Health and Clinical Excellence (NICE) on rehabilitation after critical illness promoted "optimization of recovery" of ICU patients rather than mere survival as a key therapeutic objective. It states that all patients should be assessed by intensive care unit (ICU) staff for their risk of physical and psychological morbidity.

### 2. What this study adds:

- There is even less evidence about the risk factors or underlying causes of adverse psycho-social outcomes of intensive care.
- There is a lack of evidence to guide rehabilitation efforts, about the health related quality of life (HRQL) of intensive care patients and about the prevalence, nature and extent of psychological morbidity.



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## Introduction

As the medical specialty of intensive care has developed over the past fifty years, several lives of seriously ill people have been saved. Due to advances in the prevention and reversal of organ failure, it has become possible to keep some of the sickest patients, who previously could not have survived, alive [1].

Critical illnesses and Intensive Care Unit (ICU) therapies expose patients to extreme stressors, including respiratory insufficiency, pain with endotracheal intubation and suctioning, release of inflammatory cytokines, strain on the hypothalamic-pituitary-adrenal (HPA) axis, administration of exogenous catecholamines, and delirium with associated psychotic experiences, all in the context of a limited ability to communicate and reduced autonomy. Critical illnesses are also, by definition, life-threatening, and many patients recall extremely frightening ICU experiences [1].

Patients' health-related quality of life (HRQL) or well-being will be affected by their physical, cognitive and psychological state. In addition to physical problems such as muscle weakness, breathlessness and the inability to eat, former intensive care patients may also suffer from cognitive impairment, anxiety, post-traumatic stress disorder (PTSD) or depression [2].

Clinicians are interested in discovering more about these psycho-social outcomes and intervening to improve them. A clinical guideline from the British National Institute of Health and Clinical Excellence (NICE) on rehabilitation after critical illness promoted "optimization of recovery" of ICU patients rather than mere survival as a key therapeutic objective [3]. It states that all patients should be assessed by intensive care unit (ICU) staff for their risk of physical and psychological morbidity and offered rehabilitation for any problems detected both in the hospital and after discharge. However, there is a lack of evidence to guide rehabilitation efforts, about the HRQL of intensive care patients and about the prevalence, nature and extent of psychological morbidity in the months after intensive care [2].

There is even less evidence about the risk factors or underlying causes of adverse psycho-social outcomes of intensive care [3].

Patients in ICU experience treatments that cause discomfort and distress, invasive monitoring and the effects of powerful psychoactive drugs. At the same time, they are often unable to communicate (due to intubation for mechanical ventilation) and suffer both sensory deprivation and sensory overload [4]. These experiences often result in acute psychological stress, disorientation, and delirium [5].

ICU patients need additional support at all stages of their illness - in the ICU, on the hospital ward and after their return home. Discovering which patients are most

at risk of specific psycho-social outcomes may enable to intervene to help those who are most vulnerable to psychological distress and poor HRQL after leaving the ICU [5].

objective is to determine the prevalence of depression and to detect the predictors of its occurrence in ICU patients from a major public hospital in Alexandria, Egypt.

## Methods

### Subjects

We conducted a case-control study on adult patients admitted to the ICU of a governmental hospital, Alexandria, Egypt. Patients were included if they were admitted to the ICU for more than 24 hours and before discharge or within 3 days of discharge if they were awake, alert, able to communicate and orientated. Exclusion criteria were: Communication problems or sensory impairment due to e.g. deafness; patients with inability to speak, read or write; receiving palliative or terminal care; patients less than 18 years of age and receiving drug affecting cognition or with previous psychiatric illness. Also, patients with Glasgow Coma score < 15 were not included. We randomly selected patients by simple random sampling method. Those who didn't meet eligibility criteria were excluded and replaced by other randomly selected patients. We obtained the approval of the Medical Ethics Committee of Alexandria Faculty of Medicine. Consents from the patients were taken for participation in the study.

**Procedure:** We detected the prevalence of depression in ICU patients using the Arabic version of Hamilton scale [6]. We included 159 patients. Of these, 46% of the patients were diagnosed with depression compared to 53% of depression-free patients. The participation rate was 100%. The diagnosis was done by well-trained physicians on Hamilton scale other than the authors to avoid bias. Patients who had score 19 and above were diagnosed as depressed. Patients with and without depression were investigated for demographic characteristics, the length of stay, mechanical ventilation, drug intake including steroids, sedatives and vasopressors and history of cardiac arrest.

**Measurement:** We assessed patients using the Arabic version of Hamilton Depression Rating Scale (HDRS). The Arabic version of this scale was previously assessed and proved to be reliable in terms of test-retest reliability (intra-class correlation coefficient: 0.807;  $P < 0.001$ ). With regards to internal consistency, the Cronbach's  $\alpha$  value ranged between 0.607-0.756 [7].

### Statistical methods

Quantitative data were described by mean and median as measures of central tendency & standard deviation, minimum and maximum as measures of dispersion, while categorical variables were summarized

by frequency and percent. Chi-square test was used to study the significant association between two categorical variables. Fisher exact test was used if more than 20% of total expected cell counts < 5. Independent sample t-test was used to detect significant differences in the mean quantitative variables between two groups of patients. The choice of this test depended on the normal distribution of variables by Kolmogorov-Smirnov test and large sample size > 30 per group. A multivariate logistic regression analysis was done after univariate analysis to estimate the magnitude of the association between each predictor and depression occurrence, Odds ratios (OR) and the corresponding 95% confidence intervals (CI) were computed. We included the following predictors in the regression model; Sex (reference male), Age as a quantitative variable, Presence of mechanical ventilation (reference no), occurrence of cardiac arrest (reference no), intake of at least two drugs of either Steroids, sedatives or vasopressors (reference one drug intake or no intake). We assumed that multiple drugs' intake is a potential risk factor for depression rather than single or no drug intake. All statistical tests were judged at .05 significance level. Statistical analysis was done using SPSS statistics program version 21 and R software.

## Results

Table 1 shows the distribution of key variables among patients with and without depression including: gender, age in years, length of stay in days, mechanical ventilation, cardiac arrest and intake of steroids, sedatives or vasopressors. There was a female predominance (71.6%) in depressed group (< 0.001). Mean age significantly differed between the non-depressed group (49 ± 15) compared to depressed group (55 ± 15) (p < 0.05). The mean length of ICU stay was significantly higher in depressed than non-depressed group (p < 0.001). The majority of depressed patients were previously mechanically ventilated relative to one-third of non-depressed patients (p < 0.001). There was a significant association between drug intake whether steroids, sedatives or vasopressor intake and depression as an outcome (OR: 4.09 (1.8-9.1), 4.5 (2.3-8.8) and 4.3 (2.1-8.5)). The proportion of depression among patients with positive history of at least two drugs intake (63.5%) was significantly higher than those with negative history of drugs (OR: 10.6 (5.3-23.8). Half of patients with depression had a positive history of cardiac arrest compared to less than one-tenth of cardiac arrest history among non-depressed patients (OR 11.1 (4.5-27.3)).

**Table 1:** Univariate analysis for comparison of different parameters between the two studied groups.

	Non depressed (N = 85)	Depressed (N = 74)	P value
Females, n (%)	13 (15.3)	53 (71.6)	< 0.001*
Age (years)			
• Mean (SD)	49.5 (15.6)	55.1 (15.7)	0.025*
• Median (min-max)	52 (23-86)	60 (18-80)	
Length of ICU stay(days)			
• Mean (SD)	6 (4)	10 (4)	< 0.001*
• Median (min-max)	5 (2-21)	9 (5-30)	
• Mechanical ventilation, n (%)	29 (34.1)	65 (87.8)	< 0.001*
• Cardiac arrest, n (%)	7 (8.2)	37 (50.0)	
Drugs			
• Steroids, n (%)	11 (12.9)	28 (37.8)	< 0.001*
• Sedatives, n (%)	28 (32.9)	51 (68.9)	< 0.001*
• Vasopressor, n (%)	19 (22.4)	41 (55.4)	< 0.001*
• At least 2 drugs, n (%)	12 (14.1)	47 (63.5)	< 0.001*

**Table 2:** Multivariate logistic regression analysis for different parameters in relation to depression outcome.

	Unadjusted OR (95% CI)	Beta (SE)	Adjusted OR (95% CI)
Female (Yes vs. No)	13.9 (6.4-30.4)	3.86 (0.73)	47.9 (13.5-254.7)
Age (years)	1.02 (1.00-1.04)	0.056 (0.019)	1.06 (1.02-1.10)
Mechanical ventilation (Yes vs. No)	13.9 (6.08-31.9)	3.03 (0.86)	20.8 (4.5-141.6)
Cardiac arrest (Yes vs. No)	11.1 (4.5-27.3)	1.33 (0.73)	3.80 (0.91-17.25)
Length of ICU stay (days)	1.20 (1.14-1.30)	-0.02 (0.066)	0.97 (0.86-1.11)
At least 2 drugs (Yes vs. No)	10.6 (5.3-23.8)	0.42 (0.80)	1.53 (0.30-7.49)

SE: Standard Error.

Table 2 illustrates the multivariate logistic regression model including unadjusted and adjusted odds ratios of the variables which were significant by univariate analysis. The model included: Age in years, sex, mechanical ventilation, history of cardiac arrest, length of stay in days and history of drug intake. The odds of depression increased by 47.9 (95% CI: 13.5 to 254.7) in females relative to males. Mechanical ventilation history was the second contributing predictor to depression (OR 20.8, 95% CI: 4.5 to 141.6). The odds of depression was about 4 times in patients with history of cardiac arrest than those with negative history (OR 3.8, 95% CI: 0.91 to 17.25). One unit (year) increase in age increased the odds of depression by 6% (OR 1.06, 95% CI: 1.02 to 1.10).

The significant association between length of stay, two drugs intake history and depression outcome in univariate analysis ( $p = 0.010^*$ ,  $< 0.001^*$ ) turned into non-significant contribution of length of stay, history of two drugs intake to occurrence of depression by regression modeling ( $p = 0.797$ ,  $0.673$ ).

## Discussion

Psychological morbidity in ICU patient is a major concern. It is therefore important to establish better measures for assessing the magnitude of this problem, its management and its prevention [3].

In our study, we focused on assessing depression in ICU patient as a primary outcome by using the Hamilton Depression Rating Scale (HDRS). The prevalence of depression was 46.5%. In other studies, depression ranged from 2.8% to 52%. This variation can be explained by a number of factors; Studies measured depression using different instruments, including The Center for Epidemiological Studies-Depression (CES-D), [8] the Hospital Anxiety and Depression Score (HADS), the Hamilton Depression Rating Scale (HDRS) [9] and the Structured Clinical Interview for DSM Disorders (SCID) [10]. In addition, some of these studies assessed depression after discharging the patient from ICU. The prevalence of depression in our study was high in comparison to most other studies. This could be attributed to differences in the source populations. Our study population was admitted patients from AMUH. Most of them were of low socioeconomic status (SES) and hence with increased risk of depression. This relation between SES and depression was seen in many studies where low SES is generally associated with high psychiatric morbidity, more disability, and poorer access to health care [11].

In multivariate analysis, each year increase in age increase risk of depression by 6%. This is in agreement with some studies, [12] although there is a relation between age and depression in the general population, not only ICU population [13].

We observed a female predominance in the depres-

sed group ( $p < 0.001$ ) both in the univariate and the multivariate analyses. This finding is consistent with a Swedish study of 226 patients interviewed to estimate the predictors of acute post-traumatic stress disorder (PTSD). In that study, being a female, increased the odds of PTSD by about 5 times than males (OR 4.74, 95% CI: 1.44 to 15.5) [14]. We interpreted the increase of female odds ratio in our study from univariate to multivariate analysis by finding a significant association between female gender and both mechanical ventilation and at least two drugs intake ( $p$  value 0.014, 0.007).

Patients with longer ICU stay were at risk of depression, but multivariate logistic regression analysis demonstrates no effect of the length of ICU stay on the psychological outcome. This observation may be due to the longer the ICU stay, the more interventions the patient had and elderly people who are more vulnerable to depression tend to stay longer in ICU due to associated comorbidities but length of ICU stay as a single factor has no effect on the outcome of depression. This is in agreement with a study from England which assessed the relation between the duration of ICU stay and psychological stress measured by the Experience after Treatment in Intensive Care 7 Item Scale (ETIC-7) [15].

Our results are in agreement with a prospective study of 78 patients from Scotland that previously mechanically ventilated patients were more prone to depression in univariate and multivariate analyses [16]. Mechanical ventilation was an independent risk factor for depression. However, a study including 37 patients followed up from Germany, found no relation between the duration of mechanical ventilation and PTSD [17]. Several studies highlighted the distressing nature of mechanical ventilation for patients [18-20]. Patients reported that the endotracheal tube was uncomfortable and remembered having their hands restrained to stop them touching the tube or being threatened with restraint. They felt they were going to suffocate during suctioning of secretions from the trachea and could not synchronize their breathing with the ventilator after suctioning. Patients frequently found the procedures of extubation and decannulation, following weaning from the ventilator, to be unpleasant and problematic [21].

Patients with previous history of cardiac arrest were at increased risk of depression about four times than those with negative history of arrest. This is consistent with a Polish study of 30 patients with sudden cardiac arrest (SCA) and 31 controls with infection without SCA [22].

Drug intake of steroids, sedatives or vasopressors was significantly associated with depression ( $p < 0.001$ ). This is in concordance with a prospective study of 157 patients from England shows a strong relation between sedatives, vasopressors but not corticosteroids and occurrence of depression [21].



Our study has many strengths but also some possible limitations. Challenges in case control design are selection bias and confounding. We considered their effect in both design by selecting the cases from the same source population of controls and in the analysis by using multivariate logistic regression. Recall and interviewer bias were unlikely to be relevant as most of included risk factors are objective e.g. mechanical ventilation history, history of cardiac arrest, sex, et al. However, our research was carried on patients from AMUH; a governmental hospital where most of patients are from low SES that may overestimate the prevalence of depression. This prevalence reflects the estimate from insurance and ministry of health hospitals where the same low SES huge population are seeking medical healthcare.

This work presses the alarm button for improving the psychological support of ICU patients. The ICU is a place that represents a high severity of illness. This necessitates the need of mental health assessment and psychological interventions applied for patients. A recent systematic review investigated the role of psychological care for relief of psychological stress in ICU. Twenty-three studies were included, and the review concluded that non-pharmacological approaches to reducing ICU distress, in particular psychological interventions, may be beneficial [23]. This support should extend to patient's families as well. One randomized controlled trial involved a communication facilitator to increase families' and clinicians' self-efficacy expectations about communication in the ICU. It proved that adjusted depression scores were significantly lower for the intervention group than for the control group [24].

## Conclusion

The prevalence of depression was high among our ICU population. Use of mechanical ventilation, history of cardiac arrest, old age and female sex are independent risk factors for depression among ICU patients.

## Ethics Approval Statements

Not applicable.

## Clinical Trial Registration

Not applicable.

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## Competing Interest

None declared.

## Conflict of Interest

The authors declare that they have no conflict of interest.

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