# Delirium in Critical Care Medicine Department in Faculty of Medicine Alexandria University incidence and relation with sepsis

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**Abstract:** The intensivist should think of delirium, or acute central nervous system dysfunction, as the brain's form of "organ dysfunction." Delirium is extremely common in intensive care unit (ICU) patients due to factors such as co morbidity, critical illness, and iatrogenesis. The delirium is extremely hazardous in older persons and is associated with prolonged ICU stay. Lack of experience about delirium& instruments which should used to diagnose it, makes its diagnosis in ICU difficult. Sepsis associated delirium is not simply an unpleasant confusion or obtundation of the patient with sepsis, but a relevant and often severe organ dysfunction that is reflected by increase in mortality. Furthermore impaired cognitive function after critical illness, particularly in patient suffering from delirium, is increasingly being recognized. Our aim was to estimate the incidence of delirium in critical care units in Alexandria University Hospital, and to find out if there was any association between delirium and sepsis. The study was conducted on 385 adult conscious patients. All selected patients have been screened for delirium by (CAM-ICU score) daily until patients died, discharged, become unfit for score, or become positive for delirium. In selected patients, their different diagnoses was recorded, and laboratory and clinical sepsis profile was taken to found the association between sepsis and delirium. The following results were obtained: Incidence of delirium in critical care units in Alexandria university hospital is 18.4%.The age of patients with delirium was significantly higher with delirium. Duration of stay in ICU in delirious patients is higher than non delirious patients.56% of pneumonia patients developed delirium in their stay in ICU. There was a significant association between sepsis and delirium in ICU, as presence of sepsis in delirious patients was higher with delirium. Incidence of delirium in intubated or mechanically ventilated patients was significantly higher. Sepsis was found to be an important risk factor for developing of delirium in ICU. Confusion assessment method in ICU (CAM-ICU) was found to be an easy, quick, and effective tool to diagnose delirium in adult and conscious ICU patients. Respiratory tract infections is a common cause of sepsis associated delirium.

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**Keywords:** delirium, CAM/ICU, sepsis**.**

## 1. Introduction

Critical care clinicians have historically been attuned to pulmonary, cardiac, and renal dysfunction as a source of morbidity and mortality in ICU patients but have underestimated the impact of brain dysfunction.(1) Delirium, a common manifestation of acute brain dysfunction in critically ill patients, is associated with poor short-term outcomes and may result in adverse sequelae years after ICU discharge.(2-4) Delirium is defined as a disturbance of consciousness and cognition that develops over a short period of time (hours to days) and fluctuates over time.(5) Recent discussions of encephalopathy and organ dysfunction secondary to sepsis fail to mention delirium as one of the clinical manifestations of central nervous system CNS dysfunction.(6,7) Delirium develops in over 80% of ICU patients, and its incidence is likely to increase in future years as older persons more frequently receive ICU care. Delirium is associated with prolonged hospital stays and medical complications that can contribute to increased mortality,(8) and it may predispose ICU survivors to prolonged neuropsychological deficits. The pathophysiology of delirium is poorly understood but multiple promising hypotheses are considered, neurotransmitter imbalance, inflammation, impaired oxidative metabolism, availability of large neutral amino acids. In non ICU populations, the development of delirium in the hospital is associated with an in-hospital mortality rate of 25%-33%, prolonged hospital stay, and three times the likelihood of discharge to a nursing home.(9) Among ICU patients, there is current evidence that delirium is a predictor of mortality in 6-months following the ICU stay.(10) The development of delirium was associated with a threefold increase in risk of death

after controlling for pre-existing comorbidites, severity of illness, coma, and a use of sedatives and analgesics medications. Also studies showed that delirium is not simply a transition state from coma to normal because delirium occurred just as often among those who never developed coma as among those who did and persisted in 11% of patients at the time of hospital discharge.(11) Delirium complicate the hospital stay of more than 2 to 3 million elderly patients per year in the united states, involving more than 17.5 million inpatient days and accounting for more than $4 billion in Medicare expenditures.(12) Exploring local incidence and relation with sepsis in our study was done.

## 2. Materials and Methods

This work was designed to study the incidence of delirium in adult conscious patients in ICU and if there is any association between delirium and sepsis in critically ill patients. This prospective observational study was conducted on 385 adult, conscious patients, who were admitted to the Critical Care Medicine Department of Alexandria Main University Hospital in the period from January 2009 to June 2009. Consents for inclusion in the study were taken from patients or their surrogates and Local Ethical Committee. The inclusion criteria were as follows: Conscious patients whether intubated or not, more than 18 years old, able to communicate and understand Arabic or English languages.

***Exclusion criteria***

It includes: deaf by history, history of neurological or psychiatric problems, presence of motor neurological deficit, presence of hepatic or renal decompansation, sedated patients (propofol, benzodiazepines), history of acute intoxication (alcoholic, or poisons), presence of severe electrolyte abnormalities (hypo, or hypernatremia), presence of meningeal irritation signs.

***Measurements***

All patients in the study were subjected to thorough history taking, complete physical examination, radiological and laboratory investigations as:

Recording for absence or presence of sepsis by the following criteria:

- Presence of 2 from 4 items of systemic inflammatory response syndrome, which include: Temperature >38ºC or <36ºC ,
- Heart rate > 90 /+beats/min, Respiratory rate >20 breaths/min or $PaCO_2$ < 32 mmHg, WBC >12,000 cells/mm3, <4000 cells/mm3, or >10 percent immature (band) forms.
- Plus presence of source of infection either by visual inspection or positive culture.

- Urine output estimation (ml/h)
- Electrocardiogram (ECG).
- Plain Chest X ray.
- Complete blood picture.
- Random blood sugar.
- Prothrombin time, partial thromboplastin time (PT, PTT),.Blood urea, serum creatinine.
- AST, ALT, arterial ammonia level, serum sodium and potassium levels (Na, K).
- Arterial blood gases.
- Length of stay in ICU " LOS" (days) was recorded For selected patients, Confusion Assessment Method (CAM-ICU) was applied daily in ICU until patients discharged, died, were unfit for test or score became positive for delirium. This test includes the following items:

1. **Acute onset or Fluctuating Course:**
   Positive if 1.A or 1.B was present (Absent/Present).
   A. Is there evidence of an acute change in mental status form the baseline?
   Or
   B. Did the (abnormal) behavior fluctuate ( i.e., tent to come and go) during the past 24 h or increase and decrease in severity as demonstrated by Fluctuation on a GCS.
2. **Inattention:**
   Positive if either score for 2.A or 2.B is less than 8 from 10 Absent Present
   Did the Patient have difficulty focusing attention as demonstrated by errors on the auditory component of the attention screening examination (letters). If the patients was able to perform this test and score is clear, result was recorded, if the patient was unable to perform this test, visual attention screening examination (pictures)
3. Disorganized thinking
   Positive if combined score is less than 4 from5 (Absent/Present).
   3.A: yes or no questions: Is there evidence of disorganized or incoherent thinking as indicated by incorrect answers to yes or no questions
   3.B: commands: We said to the patient, "Hold up this many fingers" (examiner hold 2 fingers in front of patient) "now do the same thing with the other hand" (not repeating the number of the fingers)
   Score: Patients earn 1 point if able to successfully complete the entire commands.
4. **Altered level of consciousness (Absent/Present):**
   Is the patient's level of consciousness anything other than alert, such as vigilant, lethargic, or stupor.

The test was considered positive if features 1 & 2 plus 3 or 4 are present.

Patients with positive (CAM-ICU) were considered delirious. Therefore, confirmation of

presence or absence of sepsis was done by doing the following measurements:

- Vital signs: Blood pressure, measured by syphyngomanometer, Heart rate, recorded from patients monitors. (beats/min), Respiratory rate, which had been measured clinically (breaths/min),
- Temperature, measured by using thermometer (Celsius degree), White blood cells count.
- Multiply by103/cc) Platelets count. (multiply by 103/cc).
- C-reactive protein. (mg/l)
- Serum lactate level. (mg/dl)
- Confirmation of presence or absence of sepsis in these diagnosed delirious patients was compared with the previously diagnosed patients with sepsis

All patients were classified into:

a. Delirious
b. Non- delirious

Then delirious patients were categorized into:

c. Delirium with sepsis
d. Delirium without sepsis

length of stay, mortality and diagnosis recorded for every patient.

***Statistical analysis***

**1. Arithmetic mean ( $\bar{X}$ ):**

Was calculated as follows:

$$\bar{X} = \frac{\sum x}{n}$$

Where: $\bar{X}$ = arithmetic mean
Σx = Sum of observations
n = number of observations

**2. Standard deviation (SD):**

Was calculated as follows:

$$SD = \sqrt{\frac{\sum x^2 - \frac{(\sum x)^2}{n}}{n-1}}$$

Where: Σx2 = sum of squared observations.
(Σx)2 = square of the sum of observations.
n = number of observations.

**3. "t" test:**

$$t = \frac{\bar{X}_1 - \bar{X}_2}{\sqrt{S_p^2\left(\frac{1}{n_1} + \frac{1}{n_2}\right)}}$$

$$S_p^2 = \frac{S_1^2(n_1 - 1) + S_2^2(n_2 - 1)}{n_1 + n_2 - 2}$$

Where:

$S_p^2$ = Pooled variance.

$S_1^2$ Variance of sample (1).

$S_2^2$ Variance of sample (2).

$n_1$ = Size of sample (1).
$n_2$ = Size of sample (2).
$X_1$ = Mean of sample (1).
$X_2$ = Mean of sample (2).
$S_1$ = Standard deviation of sample (1).
$S_2$ = Standard deviation of sample (2).

**4. Chi-square (X2):**

For comparison between distribution of patients according to different items of study and use this formula for calculation:

$$X^2 = \sum \frac{(O - E)^2}{E}$$

$O$ = Observed results
E = Expected results
$(O - E)^2$ = *difference* squared

Where $E = \frac{\text{Total row x total column}}{\text{Grand total}}$

**3. Results**

The present study included 385 patients who fulfilled the inclusion criteria in the period from January to June 2009. Studied patients regarding age & sex is presented in (Table 1)

Comparison between patients with delirium, and those without delirium as regards demographic data fined that the age of patients with delirium is significantly higher than those without delirium. Also duration of stay in ICU (Days) in delirious patients is significantly higher than those without delirium is presented in (Figure 1).

Distribution of studied patients according to diagnosis was presented in (Table 2 & Figure 2).

Delirium was diagnosed by confusion assessment method in ICU (CAM-ICU) to be present in 71 patients from the total number of patients, 385 studied patients in the present study. (Table 3, Figure 3.)

When patients with delirium were distributed according to diagnosis, it was found that 56% of pneumonia patients developed delirium, followed by 46.1% of bronchial asthma patients, followed by 44.4% of pulmonary edema patients, followed by 42.2% of COPD patients, followed by 17.6% of RTA patients. Followed by 9.09% of a trial fibrillation patients, followed by 7.14% of heart block patients, followed by 4.5% of ACS patients, followed by 4.54% of DKA patients.

There was only one patient with pancreatitis, and he developed delirium (100%), but this could not be valuable.

Comparison between patients with delirium and without delirium regarding incidence of sepsis were presented in (Table 4 & Figure 4). It illustrated that, 50.7% of patients with delirium had sepsis, while 35.0% of patients without delirium had sepsis. There were statistical significant differences between patients with delirium and patients without delirium regarding incidence of sepsis.

Diagnosis of the patients with delirium regarding incidence of sepsis showed that, pulmonary edema delirious patients without sepsis were significantly higher than those with sepsis, and pneumonia delirious patients with sepsis were significantly higher than those without sepsis, and acute coronary syndrome delirious patients without sepsis is significantly higher than those with sepsis.

Incidence of delirium in intubated or mechanically ventilated patients, was significantly higher than non intubated patients. (Table 5)

Comparison between delirium patients with sepsis and those free of sepsis as regards vital signs (which had been measured after diagnosis of delirium) showed that, heart rate in delirious patients without sepsis was significantly lower than those with sepsis, systolic blood pressure (mmHg) of delirious patients without sepsis was significantly higher than those with sepsis, Diastolic blood pressure in delirious patients without sepsis was significantly was lower than those with sepsis, respiratory rate in delirious patients without sepsis is significantly lower than in those with sepsis, temperature in delirious patients without sepsis was significantly lower than in those with sepsis.

Comparison between delirium patients with sepsis and those free of sepsis are regards white blood cells count (WBCs), platelet count, C reactive protein (CRP), and serum lactate level illustrated that, WBCscount of patients without sepsis was significantly lower than in those with sepsis, platelet count in delirious patients without sepsis is significantly higher than in those with sepsis, CRP in delirious patients without sepsis is significantly lower than in those with sepsis, serum lactate in patients without sepsis is significantly lower than in those with sepsis.

As regard the length of stay in ICU (LOS) in the present study, there was a high significant relation between delirium and length of stay in ICU (LOS). Duration of ICU stay in delirious patients was from (3-11)day with mean+_SD 7.36 $\pm$ 2.68 days, and in non delirious patients duration of stay in ICU was from (2-6) days with mean $\pm$ SD 4.52$\pm$2.11days were presented in (Figure 5).

**Table (1): Age & sex distribution in the studied patients.**

| | |
|---|---|
| **Age(years):** | |
| Range | 24 – 86 |
| Mean±S.D. | 61.9±19.8 |
| **Sex (number, precent %):** | |
| Male | 255(66.2%) |
| Female | 130(32.8%) |

**Table (2): Distribution (number& percentage) of delirious patients according to diagnosis among the total studied patients.**

| Diagnosis | Total Pts | Delirium Pts | % |
|---|---|---|---|
| Pneumonia | 25 | 14 | 56% |
| Bronchial asthma | 13 | 6 | 46.1% |
| Pulmonary edema | 36 | 16 | 44,4% |
| COPD | 45 | 19 | 42.2% |
| Roar traffic accidents(RTA) | 17 | 3 | 17.6% |
| Atrial fibrillation (AF) | 22 | 2 | 9.09% |
| Heart block | 14 | 1 | 7.14% |
| Acute coronary syndrome | 176 | 8 | 4.5% |
| DKA | 22 | 1 | 4.54% |
| Pancreatitis | 1 | 1 | 100% |

**Table (3): Incidence (number, percentage) of delirium among studied patients.**

| | Number | Percent |
|---|---|---|
| **Patients with delirium** | 71 | 18.4 |
| **Patients without delirium** | 314 | 81.6 |
| **Total** | 385 | 100.0 |

**Table (4): Comparison between patients with and without delirium regarding incidence of sepsis.**

| | Patients with delirium | | Patients without delirium | |
|---|---|---|---|---|
| | **No.** | **%** | **No.** | **%** |
| **With sepsis** | 36 | 50.7 | 110 | 35.0 |
| **Without sepsis** | 35 | 49.3 | 204 | 65.0 |
| **Total** | **71** | | **314** | |
| **$X^2$** | | **6.04** | | |
| **P** | | **0.0139*** | | |

**Table (5): Comparison between patients with delirium and without delirium as regards endo-tracheal intubation (ETT), mechanical ventilation.**

| | | Patients with delirium "n=71" | Patients without delirium "n=314" | Test | P |
|---|---|---|---|---|---|
| **ETT** | Yes | 40 (56.3%) | 110 (35.0%) | $X^2$ = 11.05 | 0.0008* |
| | No | 31 (43.7%) | 204 (65.0%) | | |

P* is significant < 0.05.

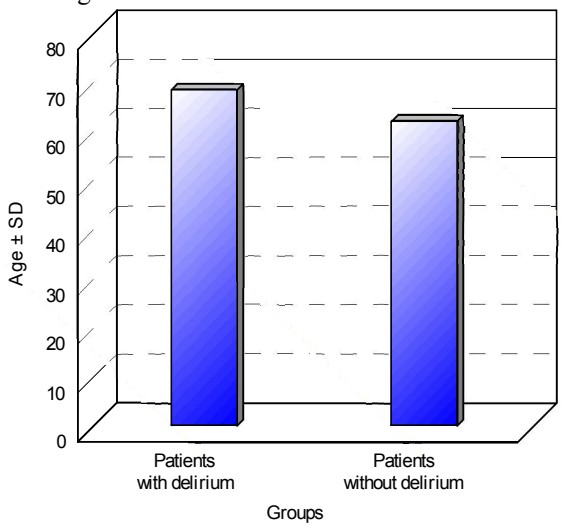


Figure 1. Comparison between patients with, and without delirium as regards age.

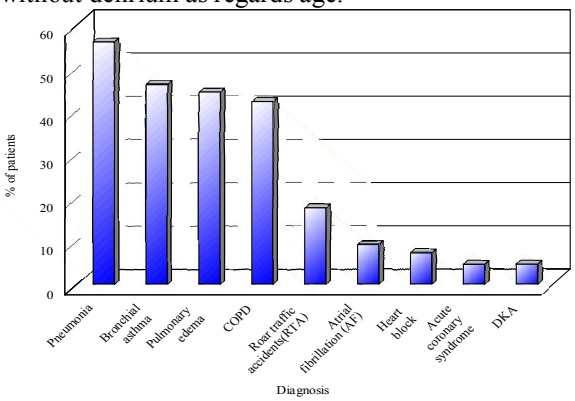


Figure 2. Distribution (number& percentage) of delirious patients according to diagnosis among the total studied patients).

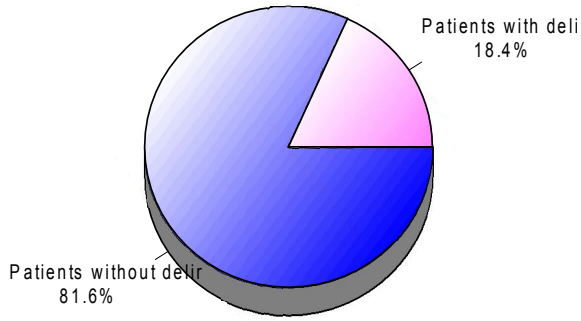


Figure 3. Incidence of delirium among studied patients.

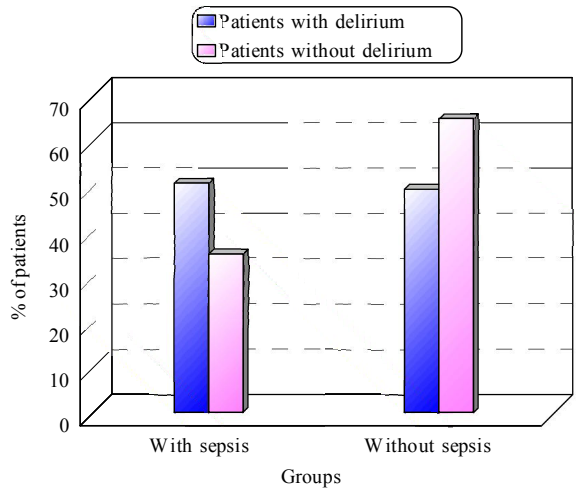


Figure 4. Comparison between patients with and without delirium regarding incidence of sepsis.

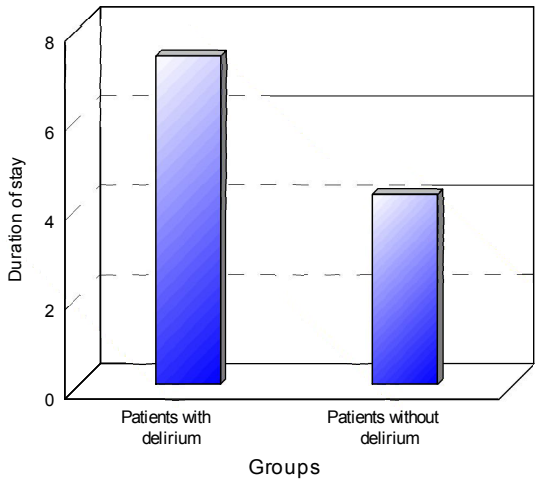


Figure 5. Comparison between patients with and without delirium as regards, duration of stay in ICU

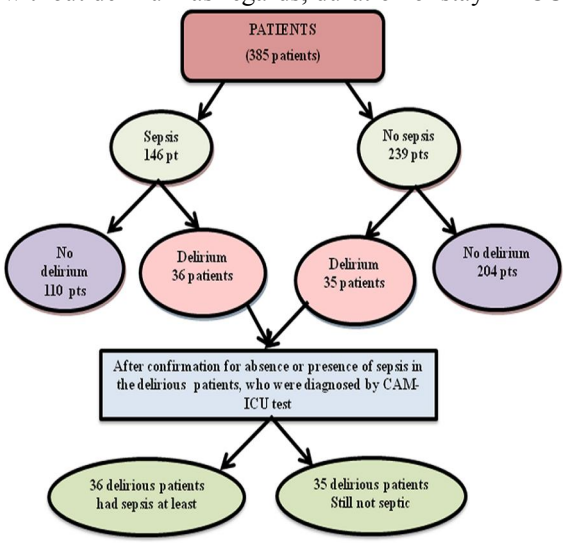


Figure 6. Diagrammatic illustration showing association between sepsis and delirium in the present study.

## 4. Discussion

In the present study, delirium was diagnosed by CAM- ICU test in 71 patients from the 385 studied patients (18.4%), this incidence is falling in the mid- range of reported international rates (15-80%)(13), presence of this relatively lower incidence of delirium in the present study may be contributed to many factors which help in prevention of delirium in ICU, but to my mind the architecture of the studied ICU (critical care unit 1, 3) might play a beneficial role in the prevention of delirium (for example, visible day light, and the distance between beds especially in critical care unit 3.

This wide range in the incidence of delirium between different ICUs may be contributed to difference in sample size, difference of duration of conduction of the researches, using of different screening tools to diagnose delirium, application of studies in medical, surgical, or mixed ICUs, different diagnoses, presence of co morbidities, influence of drugs, infusions, sedatives, and analgesics, which used frequently in ICU.

Quiment and colleague(14) found in their prospective study, which were done on 820 patients, in 16 bed medical, and surgical ICU, that incidence of delirium was 31.8%, which is higher than incidence in the present study, and this may be explained by larger number of patients included in their study, and also by using different screening tool for diagnosing of delirium (Intensive care delirium screening check list (ICDSC), which applied on patients with abnormal conscious level, and patients with neurological, or psychological problems, this is away from CAM-ICU which should be applied only in conscious patients.

There are many screening tools for diagnosis of delirium in ICU, incidence of delirium may differ according to the used screening tool. CAM-ICU test is considered a brief, accurate, and reliable instrument for use by nurses and physicians to identify delirium in ICU patients, the CAM-ICU is easy to administer, takes on average less than 1 minute to be completed, and require minimal training.(15)

Ely and co workers(15) originally validated CAM-ICU score in two cohort studies of 38 and 111 medical ICU patients, CAM-ICU had sensitivity (93-100%), and specificity (89-100%). This was in agreement with Lin et al(16) who validated CAM-ICU score in a separate cohort study of 102 mechanically ventilated patients, and reported sensitivity (91-95%), and specificity (98%). While Bergeron and colleagues(17) validate ( ICDSC score) for diagnosis of delirium in 93 ICU patients, and reported a sensitivity of 99%, specificity of 64%. In this score each patient is assigned a score from 0-8, a cut off score of 4 or less is considered delirium, (ICDSC) is different from (CAM-ICU) in that it cannot be done in intubated patients, and applied in patients with abnormal conscious level.

Another tool for diagnosing delirium in ICU, was uesd in Bartvan et al(18), which is (NEECHAM "Neelon and Champagne" confusion scale), with reported sensitivity of 87%, and specificity 95%. In this study comparison between CAM-ICU score, and NEECHAM scale for diagnosis of delirium was done on 172 non intubated mixed ICU patients (all adult patients with Glasgow coma scale " GCS" more than 9 were included), incidence of delirium by CAM-ICU was 19.8%, and by (NEECHAM) was 20.3%, so the two scores nearly equal in assessing occurrence of delirium in non intubated ICU patients.

In Valerie J et al(19) study, incidence of delirium was screened for 3 months, by application of (CAM-ICU) on 71 ICU patients. Non communicable, sedated patients were excluded, and (CAM-ICU) score was applied every 12 hours for selected patients, they found that 45% of examined patients developed delirium. The relatively high incidence of delirium in this study may be explained by small number of patients (only 71 patients) in comparison to 385 patients in the present study.

In Roberts et al(20) study, which was multicentre study of delirium in 6 ICUs in Australia and New Zealand , delirium was found to be occurred in 45% of studied 185 patients. Increasing the incidence of delirium in this study over the present study may be explained by small sample size (185 patients in this study versus 385 patients in the present study), and also by using of (ICDSC test) in diagnosing delirium in this study versus using (CAM-ICU) in diagnosing delirium in the present study.

The inclusion of patients on narcotic analgesia in the present study have contributed to the low incidence of delirium, however in Dubois and co workers(17) study , morphine was found to be one of the strongest factors of developing delirium in ICU, mostly this is due to its sedating effect. But in Quiment and colleagues(14) study, they found that mean daily opioid dose were higher among ICU patients without delirium than among those with delirium, this was in line with Morrison and colleagues(21) study, who also found that patients treated with opioids analgesia (more than 10mg/d parenteral morphine sulphate equivalent) were less likely to develop delirium than patients than patients who received less analgesia, and it may be explained by effect of pain and agitation in developing delirium in ICU.

Psychoactive drugs in ICU causes a considerable conflict as regards delirium, in Roberts et al(20) study, 45% of studied patients developed delirium, and most of them received greater amount of psychoactive drugs, in particular haloperidol, propofol, midazolam, morphine, and other psychoactive drugs, these agents and others have previously been associated with the development of delirium while in the same line used as treatment of this condition.

In this concern, it is not clearly established whether the development of delirium necessitate the use of these drugs, or the administration of these drugs cause or exacerbate delirium.

In the present study, there was significant relation between occurrence of delirium, and older ages (mean $\pm$ SD 68.4 $\pm$ 8.2 years in delirious patients, versus 61.9 + 15.6 years in non delirious patients; p= 0.046). This in agreement with findings of Kapoor et al(22) (mean $\pm$ SD 56 $\pm$ 18 in delirious patients versus 49 $\pm$ 17 years in non delirious patients; p= 0.002) .

This relation between delirium and older age may be attributed to aging process, disease of the brain, decrease of neurotransmitters particularly acetylcholine, stress, failure to adapt to residing in un familial environment, chronic diseases, vision and hearing impairment, presence of underlying cognitive abnormality such as dementia in older patients, pain, and use of multiple drugs and infusions, and use of catheters and devices such as folys catheters, central venous lines in older patients in ICU.(23)

Also in older age, sleep disturbance have a great role in developing delirium, and this had been focused in Cooper and colleagues(24) study, which conducted on 20 mechanically ventilated ICU patients. They found that there was positive correlation between incidence of delirium, and sleep disturbance in the patients, explanations was due to abnormalities occured with sleep disturbance like altered protein synthesis, impaired cellular, and humoral immunity, energy expenditure, and ultimately they may contribute to organ dysfunction such as delirium.

However in Aldemier et al(25) study, there was no relation between delirium occurance, and age, it may be explained by application of this study in surgical ICU only, which had relatively different category of patients of lower acuity, less complex co morbidities, and less pharmacological treatment. In the present study all patients were in medical ICU.

In the present study, delirium occurred in 56% of patients with pneumonia, this may be explained by their older age, and need of most of them to mechanical ventilation. Also presence of sepsis in these patients increased the risk for delirium.

This was in agreement with Raul AL et al(26) study who found 45% of pneumonia patients developed delirium in ICU, they explained this relation by increase level of ages in their patients, and presence of hypoxia in pneumonia patients. Torres et al (27), also found association between delirium and pneumonia, as 47% of pneumonia patients had delirium. They attributed this to increased age in the patients, and by use some antibiotics which may play role in developing delirium in ICU patients like levofloxacin, and clarithromycin.(28)

But in Bartvan et al(18) study, a multicentre study, which done in 4 centers, conducted on 532 ICU patients, all adults patients with GCS higher than 10 was included and screened for delirium by using (NEECHAM confusion scale), they found that patients with APACHE II score higher than 24 was high risky for developing delirium, without

specifying different diagnoses, this positive relation between delirium and severity of illness in critically patients , was explained by older age, presence of multiple and complex co morbidities, use of multiple infusions and drugs, presence of abnormal blood value levels, use of catheters, drains, and need of most of these patients to mechanical ventilation.

In the present study, there was highly significance relation between occurrence of delirium and mechanical ventilation, as 56.3% of delirious patients were mechanically ventilated, versus 35% only of non delirious patients. This mostly due to the presence of other co morbidities specially respiratory diseases such as chronic obstructive pulmonary disease (COPD) 26, 8%, pulmonary edema 22.5%, pneumonia 19,7%, and these cases mostly need mechanical ventilation in ICU.

This is in agreement with many studies. In Pratik et al(29) study, 60% of delirious patients, and in Wesley et al(30) 80% of delirious patients were mechanically ventilated, and in Rompaey et al(31) study intubated patients were risky to develop delirium in ICU.

As regard the length of stay in ICU (LOS) in the present study, there was a high significant relation between delirium and length of stay in ICU (LOS). Duration of ICU stay in delirious patients was from (3-11)day with mean+_SD 7.36+_2.68 days, and in non delirious patients duration of stay in ICU was from (2-6) days with mean +_SD 4.52+_2.11days.

This is in agreement with Roberts et al(20) study, in which the length of ICU admission was significantly higher in delirious patients thanin non delirious patients by average of 3 days.

This may indicate that delirium prolongs ICU admissions; that longer exposure to the ICU environment increase the risk of delirium; or it may be simply that patients admitted for longer duration were screened more often for delirium, and thus had more chance of being diagnosed with the condition.

Also Quiment et al(14) study, Line et al(32) study, Ely et al(33) study, and Jason et al(34) showed increase duration of ICU stay with delirium patients, and they attribute this to excessive use of sedations in critically ill patients, contrary to the present study.

But in Lin et al(32) study, which conducted on only 134 patient, there was no significant relation between delirium and increased length of stay in ICU, this contradiction to the present study may be explained by small number of the patients in this study.

In the present study, there was significant relation between patients with delirium, and those without delirium as regards presence of sepsis, more than half the patients with delirium (50.7%) have sepsis, where 35% of patients without delirium have sepsis.

Sepsis, a known or suspected infection leading to the systemic inflammatory response syndrome, frequently presents with delirium and represents perhaps the most common causal factor for ICU delirium.(35) Explanations suggest that sepsis may be a gateway to acute CNS dysfunction and brain damage via degradation of the blood-brain barrier and neuro inflammation.(36) The prevalence of coexistent delirium during sepsis ranges from 9% to 71% depending on diagnostic definitions.(37)

This is in agreement with Goyette RE et al(38) study which found profound association between sepsis and delirium and explanation was due to the potential effect of a septic inflammatory cascade to decrease essential oxygen and nutrient delivery to cells by impairing capillary blood flow .

Wheeler AP et al(39) study explained this association by elevated levels of blood mediators in sepsis like tumor necrosis factor-alpha, interleukin-1, and other cytokines and chemokines that are released in response to lipopolysaccharide can result in disseminated intravascular coagulation and promote leukocyte–vascular endothelium adhesion and induce endothelial damage at level of central nervous system (CNS)

Sharshar and colleagues(40) have suggested that sepsis-induced encephalopathy may result from degradation of the blood-brain barrier, leading to increased permeability. They recently reported that individuals who sustained septic shock exhibited abnormal MRIs with varying degrees of encephalopathy and damage to white matter tracts

Hellstrom IC et al(41) study explained sepsis associated delirium by the prolonged exposure to lipopolysaccharide in sepsis, which may impair the synaptic transmission and neuronal excitability of pyramidal neurons of the hippocampus.

From these studies, it could be suggested that the relationship between sepsis and delirium will continue to be a productive area of research. To better understand how sepsis and other acute infections may lead to delirium, it will be necessary to develop accurate biomarkers of deliriogenic processes. Unfortunately, this has proven to be a difficult task

Girrard et al(42) study found that elderly patients with delirium have an increased risk of developing sepsis, compared with patients without delirium. They explain that by presence of frequent comorbidities, institutionalization, declining performance status, and altered immune function.

In Seaman et al(43), which was conducted on 101 patient, 30 patient from them developed delirium during their ICU course. They also found that 27% of

delirious patients had sepsis, where only 6% of non delirious patients have sepsis, which confirm profound association between sepsis and delirium in ICU. The study explained this by impaired oxidative stresses in septic patients which showed in this study by measuring hemoglobin, hematocrit, oxygen saturation.

But in Eidelman et al(44) study, explanation of sepsis associated delirium was found to be due to presence of elevated blood urea level, serum bilirubin, and increase of APACHE11 score in septic patients.

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