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Delirium in patients admitted to a cardiac intensive care unit with cardiac emergencies in a developing country: incidence, prevalence, risk factor and outcome

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ABSTRACT

Aim: To assess the incidence, prevalence, risk factors and outcome of delirium in patients admitted to a cardiac intensive care unit (ICU) of a tertiary care hospital.
Methods: Three hundred nine consecutive patients admitted to a 22-bed coronary care unit were screened for presence of delirium by using Confusion Assessment Method for Intensive Care Unit (CAM-ICU), and those found positive on CAM-ICU were further evaluated by a psychiatrist to confirm the diagnosis of delirium as per *DSM-IV-TR* criteria. Patients were also evaluated for the risk factors for delirium and outcome of delirium.
Results: Incidence rate of delirium was 9.27%, and prevalence rate was 18.77%. The risk factors identified for delirium in binary logistic regression analysis were hypokalemia, Sequential Organ Failure Assessment score, presence of cognitive deficits, receiving more than three medications, sepsis, hyponatremia, presence of cardiogenic shock, having undergone coronary artery bypass grafting, left ventricular ejection fraction <30, currently receiving opioids, age more than 65years, presence of diabetes mellitus, presence of uncontrolled diabetes mellitus, history of seizures, presence of congestive cardiac failure, having undergone angioplasty, presence of atrial fibrillation, ongoing depression, currently receiving/taking benzodiazepines, warfarin, ranitidine, steroids, non-steroidal anti-inflammatory drugs, higher total number of medications, presence of raised creatinine, anaemia, hypoglycemia, Acute Physiology and Chronic Health Evaluation II score and Charlson Comorbidity Index score. About one fourth ($n=22$; 27%) of the patients who developed delirium died during the hospital stay in contrast to 1% mortality in the non-delirious group. Those with delirium also had longer stay in the ICU.
Conclusions: Delirium is highly prevalent in the cardiac ICU setting and is associated with presence of many modifiable risk factors. Development of delirium increases the mortality risk and is associated with longer cardiac ICU stay.

1. Introduction

Worldwide highest morbidity and mortality is attributed to cardiovascular diseases (CVD) [1]. Estimates suggest that there is a rising trend in CVD death worldwide. Another alarming trend suggests that cardiovascular diseases have an onset 10–15 years earlier in developing countries than in developed countries [2]. Data suggest that in developed countries, deaths related to CVD are more common in subjects with older ages, whereas in developing countries, CVD deaths are more common among the younger population [3].

A recent review suggests that, in India, cardiovascular diseases accounted for 1.4 million deaths in the year 2004, and it is projected to increase to 2.1 million in 2021 [4]. Due to this it is projected that by 2021, the number of hospitalizations due to cardiovascular diseases is going to increase by 1.62 times and the majority of these will be persons aged 25–59 years [4].

However, the reality is that developing countries like India are poorly equipped with facilities to cater to the need of all the critically ill subjects. Hence, it is expected that available resources are utilized optimally and all the needy subjects are able to receive the intensive care unit (ICU) facilities at the time of need. One way to optimally utilize available resources is to reduce the duration of ICU stay to the minimum, so that a higher number of patients can utilize the available services.

Delirium is a condition of acute brain dysfunction, which is characterized by disturbances in consciousness, orientation, memory, thought, perception, and behavior. However, delirium is often not suspected, not screened and not looked for, so it remains under-detected and misdiagnosed [5]. It is often neglected, because it is "expected" to happen in patients with severe illness, and medical resources are preferentially dedicated to managing the more immediate "life-threatening" problems. Clinicians generally give less importance to acute brain syndrome as a predictor of poorer overall outcome than acute dysfunction of other organ systems and regard it as transitory with no long-term adverse effect [6]. However, data from ICU set up including those involving patients undergoing cardiac surgery suggest that delirium is associated with longer ICU stay, and

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poorer functional and cognitive outcomes [7]. Due to delirium, ICU facilities are consumed for longer duration by those suffering from the same and, resultantly, many other needy patients suffer too.

The epidemiology of delirium in mixed cardiology and cardiac surgery ICU setup is not well established [8]. Most of the data which are available are from the Western countries, involving patients undergoing cardiac surgery or treated in the cardiology setup, and the incidence rate of delirium in such patients varies from 3% to 41.7% [7–17]. A study which evaluated 212 consecutive patients with acute myocardial infarction admitted in coronary care unit reported an incidence rate of delirium to be 5.7% [17].

However, in general, there is lack of data from India with respect to delirium, especially in patients admitted to the ICU. Only one study has evaluated the incidence and prevalence of delirium in a respiratory ICU and reported incidence and prevalence rates of 24.4% and 53.6%, respectively [18]. The risk factors identified for development of delirium included higher age, higher Acute Physiology and Chronic Health Evaluation II (APACHE-II) score and metabolic abnormalities. This study also showed that delirium was associated with significantly longer duration of ICU stay and higher mortality rates [18]. Another study which involved patients admitted to medical and cardiac ICUs, although not reporting the epidemiological data, evaluated the reliability and validity of diagnosing delirium using the Memorial Delirium Assessment Scale [19]. However, no study from India has focused on the incidence and prevalence rates, risk factors and mortality associated with delirium in cardiac ICU population. In this background, the present study aimed to (1) estimate the incidence and prevalence of delirium in patients admitted to the cardiac ICU of a tertiary care teaching hospital, (2) to evaluate the risk factors associated with development of delirium, (3) to study the outcome of delirium and (4) evaluate the factors associated with mortality in patients with delirium.

2. Methodology

The study was approved by the Institute Ethics Committee. Patients were recruited after obtaining written informed consent from patients themselves or their relatives. Informed consent was obtained from the relatives only when the patient was in delirium at the first assessment.

2.1. Setting

Study was conducted in a cardiac ICU of a tertiary care teaching hospital. The cardiac ICU is a 22-bed unit which is equipped to handle patients requiring mechanical ventilation and continuous monitoring. Usually about one third to one fourth of the patients are on ventilator at any time and others are on continuous monitoring but not requiring mechanical ventilation. Most of the patients who are not on mechanical ventilation are cooperative for clinical interview. The usual patient profile of patients in the cardiac ICU includes patients presenting to the cardiac emergency with myocardial infarction, unstable angina, congestive cardiac failure, patients in a decompensated state waiting to undergo coronary angiography or angioplasty, patients who have undergone coronary angiography or angioplasty, patients with cardiac conduction defect and patients who are waiting to undergo or have undergone balloon vulvotomy. Usually the patients stay in the cardiac ICU for 24–96 h and once stable are either shifted to cardiology ward or discharged.

2.2. Design

The study followed a prospective design. Each patient meeting the selection criteria was assessed daily throughout their cardiac ICU stay until detected to have delirium.

2.3. Selection criteria

All consecutive patients admitted to the cardiac ICU during the 2-month period (May 16, 2010, to July 16, 2010) were screened for delirium subject to fulfillment of the selection criteria. Patients who are deaf were excluded.

3. Procedure

The patients and/or caregiver of all the patients admitted to cardiac ICU and available at the particular time of the day (between 5 and 9 p.m.) were approached for consent for inclusion in the study. All the patients (in case of an uncooperative patient, a relative) who provided written informed consent were assessed. The information was collected from the patient, caregivers, treating physician and nurses to reach the final conclusion about the diagnosis of delirium and depression. Assessments were carried out at a fixed time period (5–9 p.m.) of each day for assessment of delirium. Patients were assessed every day until the time they were found to be positive for delirium during their cardiac ICU stay or discharged. Pre-existing cognitive deficits were evaluated by using short-IQCODE based on the information provided by the caregivers.

Every patient meeting the selection criteria was first evaluated on the Richmond Agitation and Sedation Scale (RASS) on the day of admission. Those patients, who were rated 3 through 4 (i.e., arousable on verbal stimulation) on RASS, were assessed for delirium by using the Confusion Assessment Method for Intensive Care Unit (CAM-ICU). If a patient was found to be positive on the CAM-ICU, she/he was further assessed on *DSM-IV-TR* criteria to confirm the diagnosis of delirium by a psychiatrist. Additionally, the psychiatrist also evaluated the patient for lifetime and current major depressive disorder as per *DSM-IV-TR* criteria based on the information provided by the caregivers, patients themselves and scrutiny of treatment records.

The APACHE-II scores were recorded on the day of admission. The risk factor checklist was completed based on the information recorded in the case notes and that provided by the caregivers, the treating team and the patient wherever possible on the day of admission and subsequently updated depending on clinical status. Sequential Organ Failure Assessment (SOFA) and Charlson Comorbidity Index scores of the day on which the patient was found to have delirium for the first time were recorded.

Any patient who was rated as unresponsive at the first assessment was reassessed on the next day and every subsequent day throughout the ICU stay to ascertain his level of sedation and agitation using Richmond Agitation and Sedation Scale. If at any stage she/he was found to be arousable, then she/he was assessed on CAM-ICU to ascertain delirium and, if found positive for delirium, was assessed on *DSM-IV-TR* criteria by a psychiatrist for delirium and depression. The risk factor checklist, SOFA score and Charlson Comorbidity Index score were updated at the time the patient was found positive for delirium.

Further, all the patients were followed up throughout their hospital stay to record their clinical outcome (i.e., delirium resolved, delirium improved, delirium persisting as before, delirium worsened and death).

4. Instruments

4.1. Richmond Agitation and Sedation Scale (RASS) [20]

The RASS was used to assess sedation and agitation. It is a 10-point scale with four levels of anxiety or agitation (+1 to +4), one level to denote a calm and alert state (0) and 5 levels to assess the level of sedation (−1 to −5). A score of −4 indicates that the patient is

unresponsive to verbal stimulation and finally culminating in unarousable states (−5). It has good inter-rater reliability and validity.

4.2. CAM-ICU [21]

CAM-ICU was developed specifically for use in non-verbal (i.e., mechanically ventilated) patients. It can be administered only if the patient is arousable to voice without the need for physical stimulation. When administered by a trained health care professional, the CAM-ICU takes only 1–2 minutes. It has a minimum of 93% sensitivity and 89% specificity for detecting delirium in comparison to full *DSM-IV* assessment. In this study CAM-ICU was administered by a psychiatrist (S.L.).

4.3. DSM-IV-TR [22] criteria for delirium and major depressive disorder

DSM-IV-TR criteria for delirium are considered to be standard criteria for making the diagnosis of delirium. *DSM-IV-TR* criteria was also used to evaluate for major depressive disorder (lifetime and current). The psychiatrist (A.S.) who administered the *DMS-IV-TR* was blind to the CAM-ICU diagnosis of the fellow psychiatrist.

4.4. Risk factor checklist

A risk factor checklist was specifically designed for this study based on the review of literature with respect to risk factors for delirium in cardiac patients. All the variables included in the risk factor checklist were rated as 'present' or 'absent'. The variables which have been incorporated in the checklist include age>65 years; smoker; history of delirium in the past; history of alcohol dependence, myocardial infarction, congestive cardiac failure and peripheral vascular disease; history of stroke, history of diabetes mellitus, currently uncontrolled diabetes mellitus, seizures, investigation findings or clinical monitoring suggestive of hypoglycemia abnormal albumin level, acute infection, arterial fibrillation, ventricular arrythmias, hypernatremia, hyponatremia, hyperkalemia, hypokalemia, hypercalcemia, hypocalcemia, anaemia, increased urea levels (>40), increased creatinine levels, left ventricular ejection fraction <30%, evidence of cardiac intervention in recent past in the

Table 1
Sociodemographic profile, clinical profile, comorbidity and treatment profile of patients with and without delirium

Variables	Delirious*n*=81	Non delirious*n*=228	chi-Square test value/t value (*P* value)
Age in years	61.69±13.46 (range, 28–88)	57.01±12.7 (range, 21–86)	2.8 (.005)
≥65 years of age	40 (41.53%)	74 (32.37%)	7.35 (*P*=.007)
Sex			
Male	51 (62.96%)	30 (37.03%)	1.43 (.231)
Female	160 (70.1%)	68 (29.82%)	
Education in years	7.87±5.64 (range, 0–16)	9.70±5.01 (range, 0–21)	19.41 (.96)
Reason for admission to ICU			
Management of acute illness	78 (96.29%)	205 (89.91%)	3.16 (.075)
Planned for cardiac procedure/surgery	3 (3.07%)	23 (9.8%)	
Primary cardiac ailment			
Coronary artery disease	30 (37.03%)	156 (68.48%)	24.56 (.0001)
Coronary artery disease with other physical illnesses	37 (45.67%)	53 (23.24%)	14.57 (.0001)
Primarily a cardiac conduction disturbance — arrhythmia/heart block	4 (4.93%)	11 (4.82%)	0.002 [a] (.96)
Rheumatic heart disease with or without conduction disturbances	10 (12.34%)	8 (3.50%)	8.50 (.003)
Psychiatric illness			
History of depression in the past	4 (49.3%)	9 (3.94%)	0.004[a] (.95)
History of depression at present	37 (45.67%)	76 (33.33%)	3.92 (.047)
APACHE score	14.81±5.41 (range,5–30)	7.15±2.59 (range,0–15)	16.69 (.0001)
SOFA score	4.49±2.06 (range,1–10)	0.12±0.34 (range,0–2)	290.96[b] (.0001)
Charlson Comorbidity Index	1.80±0.95 (range, 1–5)	1.26±0.46 (range, 1–3)	6.67 (.0001)
Medications prior to developing delirium			
Ionotropes	40 (49.38%)	27 (11.84%)	49.60 (.0001)
Antibiotics	79 (96.29%)	118 (87.7%)	52.23 (.0001)
Steroids	44 (54.32%)	59 (25.87%)	21.76 (.0001)
Anticoagulant	75 (92.59%)	201 (88.15%)	1.23 (.26)
Sedatives	72 (88.88%)	179 (78.50%)	4.2 (.039)
Antipsychotics	0 (0%)	3 (1.31%)	FE=0 .57
Diuretics	75 (92.59%)	170 (74.56%)	11.83 (.0006)
Hypoglycemic	37 (45.67%)	53 (23.28%)	14.56 (.0001)
Antihypertensive	72 (88.88%)	204 (89.4%)	0.021 (.88)
Hypolipidemic	74 (91.35%)	210 (92.10%)	0.45 (.83)
Antiarrhythmic	8 (9.8%)	5 (2.19%)	6.95[a] (.008)
Ranitidine	43 (51.08%)	60 (26.31%)	19.27 (.0001)
NSAIDS	33 (40.70%)	53 (23.24%)	9.1 (.002)
Iron supplementation	18 (22.22%)	15 (6.57%)	15.33 (.0001)
Multivitamin	28 (34.56%)	55 (24.12%)	3.31 (.06)
Calcium supplements	22 (27.16%)	39 (17.10%)	3.81 (.05)
Mean number of medications without supplements	8.04±1.78 (range, 3–11)	5.90±2.05 (range, 2–11)	8.34 (.0001)
>3 medications	80 (89.76)	198 (86.8%)	8.13[a] (.004)
>4 medications	79 (97.53%)	176 (77.19%)	15.76[a] (.0001)
>5 medications	75 (93.75%)	145 (63.5%)	24.5 (.0001)
Mean number of medications with supplements	8.88±1.89 (range,4–13)	6.38±2.26 (range,1–13)	8.9 (.0001)

FE, Fisher's Exact value.
[a] chi-Square value with Yates Correction.
[b] Mann–Whitney *U* value.

Table 2
Risk factors for development of delirium in study sample

Risk factors	Total frequency	Delirious (n=81)N (%)	Non delirious (n=228)N (%)	chi-Square test value (P value)
≥ 65 Years of age	114 (36.9%)	40 (41.53%)	74 (32.37%)	7.35 (.006)
H/O stroke	7 (2.3%)	6 (9.23%)	1 (0.40%)	10.15[a] (.001)
K/C of diabetes mellitus	90 (29.12%)	37 (45.67%)	53 (23.24%)	14.57 (.0001)
Uncontrolled diabetes mellitus	64 (20.71%)	27 (33.33%)	37 (16.22%)	10.64 (.001)
H/O Seizures	1 (0.32%)	1 (1.20%)	0 (0%)	FE=0.62
Cardiac events				
Myocardial Infarction	267 (86.4%)	64 (79.01%)	203 (89.0%)	5.11 (.02)
Congestive cardiac failure	52 (16.82%)	27 (33.33%)	25 (10.96%)	21.36 (.0001)
Peripheral vascular disease	2 (.6%)	1 (1.53%)	1 (0.40%)	FE=0.45
Currently in cardiogenic shock	30 (9.70%)	21 (25.92%)	9 (3.94%)	32.93 (.0001)
Undergone (CABG)[b]	15 (4.2%)	10 (3.07%)	5 (4.50%)	11.23[a] (.0008)
Angiography	277 (89.64%)	65 (80.24%)	212 (73.61%)	10.44 (.001)
Angioplasty	200 (64.72%)	64 (79.0%)	136 (59.64%)	9.81 (.001)
LVEF[c]<30%	10 (3.2%)	7 (10.76)	3 (1.22%)	8.03 (.004)
Current Atrial fibrillation	16 (6.79%)	9 (14.81%)	7 (3.94%)	7.87 (.005)
Current Ventricular arrhythmia	10 (8.73%)	5 (14.81%)	5 (6.57%)	1.82 (.17)
Psychiatric History				
H/O delirium in past	11 (3.55%)	2 (2.46%)	9 (3.94%)	0.07[a] (.78)
H/O depression[d]	13 (4.20%)	4 (4.93%)	9 (3.94%)	0.004[a] (.95)
Ongoing depression	113 (36.5%)	37 (45.67%)	76 (33.33%)	3.41 (.06)
H/O cognitive deficit (IQCODE)[e]	26 (9.38%)	17 (22.22%)	9 (4.82%)	22.52 (.0001)
Smoker (current or past)	113 (36.3%)	26 (32.0%)	87 (30.20%)	0.94 (.33)
Alcohol dependence (current or past)	129 (41.5%)	29 (35.80%)	100 (43.85%)	1.59 (.20)
Medications				
Currently receiving benzodiazepines	225 (72.81%)	69 (85.18%)	156 (68.42%)	8.48 (.003)
Currently receiving antiepileptics	1 (0.3%)	1 (1.53%)	0 (0%)	FE=0.62
Currently receiving opioid	71 (22.97%)	44 (54.32%)	27 (11.84%)	60.93 (.0001)
Receiving warfarin	27 (8.73%)	16 (19.75%)	11 (4.82%)	16.70 (.0001)
Receiving Frusemide	57 (18.44%)	34 (14.97%)	23 (10.0%)	42.39 (.0001)
Ranitidine	101 (32.6%)	42 (51.85%)	59 (20.4%)	18.32 (.0001)
Antiparkinsonian agent	5 (1.61%)	4 (4.93%)	1 (0.43%)	FE=0.017
Steroids	102 (33.00%)	44 (54.32%)	58 (25.43)	22.54 (.0001)
Non-steroidal anti-inflammatory drugs	85 (27.5%)	32 (39.50%)	53 (18.40%)	7.92 (.004)
Antibiotics	277 (89.6%)	78 (96.29%)	199 (69.09%)	4.30[a] (.038)
Medications for Urinary symptoms	6 (1.9%)	2 (3.07%)	4 (1.63%)	FE=0.65
Ionotropes	67 (21.7%)	40 (49.38%)	27 (11.84%)	16.95 (.0001)
>3 medications	278 (89.96%)	80 (98.76%)	198 (86.8%)	8.13[a] (.004)
>4 medications	255 (82.5%)	79 (97.53%)	176 (77.19%)	15.76[a] (.0001)
>5 medications	220 (71.2%)	75 (93.75%)	145 (63.5%)	24.5 (.0001)
Sepsis				
Evidence of acute infection	105 (33.9%)	59 (72.83%)	46 (20.17%)	73.89 (.0001)
Laboratory abnormalities				
Hypernatremia (>150 mmol/L)	1 (0.3%)	0 (0%)	1 (0.40%)	**FE**=0.71
Hyponatremia (<130 mmol/L)	19 (6.14%)	17 (20.98%)	2 (0.87%)	38.47[a] (.0001)
Hyperkalemia	3 (1%)	2 (3.07%)	1 (0.40%)	**FE**=0.169
Hypokalemia (<3.5 mmol/L)	36 (11.65%)	35 (43.2%)	1 (0.43%)	102.1 (.0001)
Hypocalcemia (<8.5 mg/dl)	5 (6.17%)	3 (3.7%)	2 (0.8%)	**FE=0.115**
Abnormal albumin (g/dl)	0 (0.0%)	0 (0.0%)	0 (0%)	-
Increased urea >40 (mg/dl)	16 (5.17%)	13 (16.04%)	3 (1.31%)	23.5 (.0001)
Increased creatinine levels (>1.2mg/dl)	13 (4.20%)	12 (14.81%)	1 (0.43%)	27.18 (.0001)
Anemia[f]	33 (10.67%)	18 (22.22%)	15 (6.5%)	15.33 (.0001)
Hypoglycemia (3.9 mmol/L)	5 (1.61%)	3 (3.7%)	2 (0.8%)	**FE=0.115**
Physiological parameters				
Temperature disturbances[g]	44 (14.23%)	22 (27.16%)	22 (9.6%)	15.00 (.0001)
Acid base imbalance[h]	29 (9.38%)	23 (28.39%)	6 (2.63%)	46.64 (.0001)
Hematocrit (%) < 0 and >46	10 (3.23%)	7 (8.64%)	3 (1.31%)	8.03[a] (.004)
Other risk factors				
Use of restraints	1 (0.3%)	0 (0%)	1 (0.40%)	FE=1.00
Prolonged intubation	5 (1.6%)	4 (6.15%)	1 (0.40%)	FE=.005

[a] chi-Square with Yates correction value; FE, Fisher's Exact value.
[b] Coronary artery bypass graft.
[c] Left ventricular ejection fraction.
[d] Based on detailed evaluation by the psychiatrist as per DSM-IV TR criteria.
[e] Cognitive deficit was considered when the mean item IQCODE score was more than 3.3 indicative of cognitive decline and predict the future development of dementia.
[f] Anemia was defined as hemoglobin levels of <12 gm percent for females and < 13 gm percent for males.
[g] Hypo or hyperthermia (<34°c or >39°c).
[h] Acid base imbalance as (pH <7.15 or > 7.7).

form of angiography, angioplasty, coronary artery bypass graft surgery, evidence of cardiogenic shock, medication history of using/receiving benzodiazepines for >2weeks, antiepileptics, opioids, warfarin, furosemide, antiparkinsonian agents, steroids, non-steroidal anti-inflammatory agents, histamine blocking agents (e.g., ranitidine), antibiotics, urinary incontinence drugs, total number of

medications (>3) excluding nutritional supplements, history of cognitive deficits, use of restraints and prolonged intubation.

4.5. Short Informant Questionnaire on Cognitive Decline in the Elderly (Retrospective IQCODE) [23]

It is a 16 item instrument that evaluates the cognitive status for a period of 6-month prior to current assessment and is based on the input of a key relative. The scale is scored by adding all items and dividing the total score by 16 to get a mean score per item. The suggested cutoff for suspected dementia is a score>3.31 – 3.38.

4.6. Charlson Comorbidity index [24]

The Charlson co-morbidity index predicts the 10-year mortality for a patient who may have a range of co-morbid conditions such as heart disease, Acquired Immunodeficiency Disease or Cancer (a total of 22 conditions). Each condition is assigned a score of 1, 2, 3 or 6 depending on the risk of dying associated with this condition. All the scores are summed up to arrive at a total score which predicts mortality.

4.7. Acute Physiology and Chronic Health Evaluation II (APACHE-II) scores [25]

APACHE-II was designed to measure the severity of disease for adult patients admitted to ICUs. It is based on 12 routine physiological parameters (such as blood pressure, body temperature, heart rate etc) during the first 24hours after admission, information about previous health status and some information obtained at admission (such as age). After the initial score has been determined within 24hours of admission, no new score can be calculated during the hospital stay.

4.8. SOFA score [26]

SOFA is a scoring system to determine the extent of a person's organ function or rate of failure. It is used to assess organ dysfunction or failure over time and is useful in evaluation of morbidity. The score is based on six different parameters, one each for the respiratory, cardiovascular, hepatic, coagulation, renal and neurological systems. Sequential assessment of organ dysfunction during the first few days of ICU admission is a good indicator of prognosis. Both the mean and highest SOFA scores are particularly useful predictors of outcome. Independent of the initial score, an increase in SOFA score during the first 48hours in the ICU predicts a mortality rate of at least 50%.

5. Statistical analysis

Data were analyzed using the mean, standard deviation, frequency and percentages. Comparisons were done by using t-test, Mann Whitney U test, Chi-square test and Fisher Exact test. Binary logistic regression analysis was carried out to study the predictors of delirium and mortality. For this presence or absence of delirium/mortality was entered as a dependent variable and all the risk factors which differed significantly were entered as independent variables.

6. Results

During the study period 321 patients were admitted in ICU of which 309 (96.26%) were screened for delirium. Twelve cases couldn't be screened because they were not available in the Cardiac ICU at the specified time (i.e., between 5 to 9PM) of the day.

6.1. Incidence and Prevalence of Delirium

On CAM-ICU, 89 (28.80%) patients screened positive for delirium. All the patients were also evaluated on DSM-IVTR criteria for delirium and the diagnosis was confirmed in the 81 (26.21%) patients. Eight cases who were considered to have delirium as per CAM-ICU, did not fulfill the diagnosis of delirium as per DSM-IVTR. However, none of patients who screened negative on CAM-ICU was diagnosed as having delirium as per DSM-IVTR criteria. Of 309 patients, 58 (18.77%) patients had delirium at the first assessment (i.e. within 24hours of admission in Cardiac ICU) and were classified as 'prevalence cases' of delirium. Another 23 (9.27%) out of 248 cases developed delirium after 24hours of Cardiac ICU stay and were considered as 'incidence cases' of delirium. The prevalence cases accounted for 71.6% of all delirium cases and incident cases accounted for 28.4% of cases.

6.2. Sociodemogrpahic and Clinical profile of the participants

The sociodemographic and clinical profile of the study sample is shown in Table 1. Patients who developed delirium were significantly older and higher percentage of them were aged ≥65years. Those who developed delirium had higher prevalence of coronary artery disease with comorbid physical illness i.e., diabetes mellitus, less frequently had coronary artery disease without comorbid chronic physical illness and rheumatic heart disease. Those with delirium also had history of depressive episode at the time of admission or just prior to admission to Cardiac ICU, had significantly higher APACHE-II score, SOFA score and Charlson Comorbidity Index score. No significant differences emerged on other variables. Those who developed delirium were more frequently receiving ionotropes, antibiotics, steroids, diuretics, hypoglycemic, antiarrhythmics, ranitidine, Non-steroidal anti-inflammatory drugs and Iron supplementation. Those with delirium were also receiving higher mean number of medications and higher percentages of them were receiving 3–5 medications.

All the patients admitted to Cardiac ICU were evaluated for risk factors for delirium by using a risk factor checklist specifically designed for this study, where each factor was rated as 'present' or 'absent' depending on its presence or absence at the time of development of delirium. As is evident from Table 2, those who developed delirium were more frequently older than 65years of age, had significantly higher frequency of history of stroke in the past, more frequently had history of diabetes mellitus and current uncontrolled diabetes mellitus. Those who had delirium also had significantly higher frequency of congestive cardiac failure, myocardial infarction, cardiogenic shock, had undergone angiography/angioplasty/coronary artery bypass grafting during the Cardiac ICU stay or just prior to the same, had left ventricular ejection fraction less than 30% and current atrial fibrillation. With regard to psychiatric risk factors, those with delirium more frequently had history of ongoing depression and cognitive deficits. With regard to medications, those who developed delirium were more frequently receiving/taking benzodiazepines, opioids, warfarin, frusemide, non-steroidal anti-inflammatory drugs, antibiotics, ranitidine, antiparkinsonian drugs, antibiotics, ionotropes and were more frequently receiving 3–5 medications. In terms of laboratory parameters, those with delirium more frequently had evidence of acute infection, hyponatremia, hypokalemia, raised urea levels, raised creatinine levels and lower hemoglobin levels. Among the other risk factors, those with delirium more frequently had hyperthermia, acid-base imbalance, changes in the hematocrit and prolonged intubation.

7. Predictors of Delirium

Predictors of delirium were studied by using binary logistic regression analysis. As evident from Table 3, highest predictive values were noted for hypokalemia and SOFA score. Other risk factors which has significant predictive value for development of delirium included presence of cognitive deficits, receiving more than 3 medications, sepsis, hyponatremia, presence of cardiogenic shock, having undergone coronary artery bypass grafting, left ventricular ejection fraction

Table 3
Predictors of delirium in study sample (using binary logistic regression analysis with reference category non delirious)

Variables	*B*	Wald	Significance	Odds ratio	95% Confidence limit
Age	0.03	12.28	<0.001	1.03	1.01–1.06
Age >65	0.68	6.58	0.01	1.97	1.17–3.32
H/o stroke	−2.89	7.07	<0.001	0.05	0.00–0.46
K/C of diabetes mellitus	1.02	14.02	<0.001	2.77	1.62–4.73
Uncontrolled diabetes mellitus	0.94	10.23	<0.001	2.58	1.44–4.61
H/O seizures	22.25	0.00	1.00	4.60	0.00
Myocardial infarction	−7.69	4.94	0.02	0.46	0.23–0.91
Congestive cardiac failure	1.40	19.53	<0.001	4.06	2.18–7.55
Currently in cardiogenic shock	2.12	25.49	<0.001	8.51	3.70–19.56
Undergone cardiac intervention (CABG)	1.83	10.60	<0.001	6.28	2.07–18.98
Angiography	−1.18	9.63	<0.001	0.30	0.14–0.64
Angioplasty	0.93	9.43	<0.001	2.54	1.40–4.62
LVEF[2]<30%	2.10	9.31	<0.001	8.21	2.12–31.79
Current atrial fibrillation	1.37	6.91	<0.001	3.94	1.41–10.97
Ongoing depression	0.52	3.88	0.04	1.68	1.00–2.81
H/o cognitive deficit (IQCODE)	2.38	32.65	<0.001	10.81	4.77–24.67
Currently receiving Benzodiazepines	0.97	8.06	<0.001	2.65	1.35–5.20
Currently receiving opioid	2.18	15.82	<0.001	8.85	4.88–16.03
Receiving warfarin	1.58	14.40	<0.001	4.85	2.14–10.98
Receiving frusemide	1.86	35.07	<0.001	6.44	3.48–11.94
Ranitidine	1.12	17.54	<0.001	3.08	1.82–5.22
Steroids	1.24	21.39	<0.001	3.48	2.05–5.91
Non-steroidal anti-inflammatory drugs	0.76	7.74	<0.001	2.15	1.25–3.70
Antibiotics	−1.33	4.60	0.03	0.26	0.78–0.89
Ionotropes	−1.98	43.01	<0.001	0.13	0.07–0.24
>3 Medications	2.49	5.92	0.01	12.12	1.62–90.39
>4 Medications	2.45	11.23	<0.001	11.67	2.77–49.11
>5 Medications	1.96	19.46	<0.001	7.15	2.98–17.15
Total number of medication	0.57	46.61	<0.001	1.77	1.50–2.09
Total number of medication with supplements	0.53	50.23	<0.001	1.71	1.47–1.98
Evidence of acute infection	2.36	62.23	<0.001	10.61	5.90–19.08
Hyponatremia (<130 mmol/L)	3.40	19.99	<0.001	30.06	6.75–133.64
Hypokalemia (<3.5 mmol/L)	5.15	25.16	<0.001	172.71	23.07–1292
Hypocalcemia (<8.5 mg/dl)	−1.46	2.53	0.11	0.23	0.03–1.40
Increased creatinine levels (>1.2mg/dl)	1.40	13.73	<0.001	4.05	1.93–8.50
Anemia	1.40	13.73	<0.001	4.05	1.93–8.50
Hypoglycemia (3.9 mmol/L)	1.46	2.53	0.11	4.34	0.71–26.49
Temperature disturbances	1.25	13.87	<0.001	3.49	1.80–6.74
Acid base imbalance	−2.68	31.11	<0.001	0.06	0.02–0.17
APACHE-II Score	0.62	58.25	<0.001	1.86	1.59–2.59
SOFA Score	4.96	20.37	<0.001	143.61	16.61–1241.48
Charlson Score	1.19	29.48	<0.001	3.30	2.14–5.09

<30, currently receiving opioids, age more than 65years, presence of diabetes mellitus, presence of uncontrolled diabetes mellitus, history of seizures, presence of congestive cardiac failure, having undergone angioplasty, presence of atrial fibrillation, ongoing depression, currently receiving/taking benzodiazepines, warfarin, ranitidine, steroids, non-steroidal anti-inflammatory drugs, higher total number of medications, presence of raised creatinine, anaemia, hypoglycemia, APACHE-II score and Charlson Comorbidity Index score.

8. Outcome of Delirium

All the patients admitted to Cardiac ICU during the study period were followed up till they were discharged from the hospital or their death. About one-fourth ($n=22$; 27%) of patients with delirium died during their Cardiac ICU/hospital stay, this was in contrast to 2 patients (0.8%) in the non-delirium group, and the difference was statistically significant (chi-square value with Yate's correction 54.02****$P<.0001$). Patients with delirium also had relatively longer cardiac ICU stay [patients with delirium- mean duration of stay 2.33 (SD 2.33) vs. 1.64 (SD 1.16); t value −3.77 ($P<.001$)].

9. Risk factors for mortality in patients who developed delirium

To understand the risk factors associated with mortality, all the risk factors which were studied were compared between those who died and were discharged in the delirium group. As shown in Table 4, those who died in the hospital more frequently had comorbid diabetes mellitus, uncontrolled diabetes mellitus, accompanying infection, cardiogenic shock, disturbances of temperature, acid-base balance and were currently receiving opioids.

Among the different risk factors, presence of uncontrolled diabetes mellitus, cardiogenic shock and sepsis had highest odds ratio for predicting in hospital mortality. Other predictors of mortality in the hospital were presence of diabetes mellitus, higher APACHE-II score, Higher SOFA score and higher Charlson score (Table 5).

10. Discussion

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 on morbidity and mortality [27]. However, in recent times it is recognized that presence of delirium increases the ICU stay and mortality [12]. Due to this it is suggested that if delirium is identified and managed early, it can lead to reduction in ICU stay [28]. The first step in this direction is to understand the incidence, prevalence, risk factors and outcome of delirium. Understanding the incidence, prevalence, risk factors and outcome can sensitize the clinicians attending these subjects and lead to early and proper identification, adequate treatment and

Table 4
Comparison of risk factors for delirium in those who died and who were alive at the last assessment in the hospital

Risk factors	Death in the hospital*n*=22N (%)	Alive at discharge*n*=59N (%)	chi-Square test (p-value)
K/C of diabetes mellitus	14 (63%)	23 (40%)	3.92 (.047)
Uncontrolled diabetes mellitus	18 (81%)	9 (15%)	29.02[a] (.0001)
Currently receiving opioid	8 (24%)	36 (61%)	3.92 (.047)
Evidence of acute infection	20 (90%)	39 (66%)	3.81[a] (.05)
Currently in cardiogenic shock	21 (95%)	0 (0%)	FE=0.0001
Temperature disturbances	22 (100%)	10 (16%)	42.83 (.0001)
Arterial pH	22 (100%)	10 (16%)	42.83 (.0001)
APACHE-II Score	20.31±4.31	12.76±4.23	7.10 (.0001)
SOFA Score	6.36±2.15	3.79±1.50	6.06 (.0001)
Charlson Comorbidity Index	2.31±1.28	1.61±0.71	3.12 (.0025)

[a] chi-Square test with Yates Correction.

reduction in overall ICU stay. The current study was an attempt in same direction.

To the best of our knowledge, this is possibly the first study from India, which has evaluated the incidence and prevalence of delirium among patients admitted to cardiac ICU. This study involved all the consecutive subjects admitted to the cardiac ICU during the period of 2 months. All the subjects were assessed at a specified time of the day (5–9 p.m.) throughout their cardiac ICU stay, to pick up cases of delirium, to take care of the diurnal fluctuation of symptoms and to maintain homogeneity of assessments. The longitudinal assessments during the hospital stay provided an opportunity to study outcome of delirium prospectively. All the participants were followed up during their hospital stay to study the outcome in terms of death and duration of ICU stay. The methodology followed in the current study tried to overcome some of the limitations of existing literature in the form of obtaining longitudinal assessment, careful screening on RASS and CAM-ICU, confirmation of diagnosis of delirium based on *DSM-IV-TR* diagnostic criteria by a psychiatrist, studying the risk factors for development of delirium and outcome of patients admitted to cardiac ICU.

Most of the patients evaluated in this study were younger than 65 years, which supports the notion that in a developing country like India, cardiovascular diseases are more frequently seen in younger populations [4].

10.1. Incidence and prevalence of delirium

During the 2-month study period, 321 patients were admitted in cardiac ICU, of which 309 (96.26%) were screened for delirium, which suggests that only a minority of patients could not be assessed. Hence, it can be said that the findings of the study can be generalized to our setting and other settings alike. On CAM-ICU, 89 patients (28.80%) screened positive for delirium on CAM-ICU. When evaluated on *DSM-IV-TR* criteria, diagnosis was confirmed in 81 patients (26.21%). However, none of patients who screened negative on CAM-ICU was diagnosed as having delirium as per *DSM-IV-TR* criteria. Majority of the cases of delirium (*n*=58; 18.77%) were those of prevalence, i.e., diagnosed with delirium at the first assessment done within 24 hours of admission in cardiac ICU. Another 23 (9.27%) out of 248 cases found to be negative for delirium at the first assessment developed delirium after 24 h of cardiac ICU stay and were considered as "incidence cases" of delirium. The prevalence cases accounted for 71.6% of all delirium cases, and incident cases accounted for 28.4% of cases.

As there are no studies from other parts of the world which have specifically evaluated the prevalence of delirium in patients admitted to cardiac ICU, catering mainly to the cardiology patients, we cannot compare the prevalence data with the cardiology patients. However, the prevalence rate found in this study is in the broad range of 20–80% reported in other ICU settings [29]. The incidence rate of 9.27% is in the range (3–41.7%) reported from the Western countries, involving patients undergoing cardiac surgery or treated in the cardiology setup [7–17]. From this it can be concluded that incidence of delirium in cardiac ICUs is similar across different countries and the minor differences are possibly determined by the clinical profile of the patients.

Findings of incidence and prevalence of delirium in the present study are lower than those seen in the respiratory ICU setting. These differences possibly could be due to severity of illness which is reflected by the fact that the mean APACHE-II score of patients who developed delirium in previous study was about 20; in contrast, in the present study, the mean APACHE-II score of patients who developed delirium was 14.8. Similarly the mean APACHE-II score of non-delirium patients was also lower in the present study compared to that reported by Sharma et al. [12].

Table 5
Predictors of death (ICU) in delirium group (using binary logistic regression analysis with reference category alive)

Variables	B	Wald	Significance	Odds ratio	95% Confidence limit
Age	−0.04	5.97	0.01	0.95	0.91–0.99
Age >65year	−1.03	3.94	0.04	0.33	0.11–0.98
K/C of diabetes mellitus	1.00	3.79	0.05	2.73	0.99–7.55
Uncontrolled diabetes mellitus	3.21	23.72	<0.001	25.00	6.84–91.28
Currently receiving opioid	−1.00	3.79	0.05	0.36	0.13–1.00
Evidence of acute infection	1.63	4.27	0.03	5.12	1.08–24.16
Currently in cardiogenic shock	25.28	0.00	0.99	9.53	0.00
Temperature disturbances	−3.15	24.06	<0.001	0.04	0.02–0.15
Arterial pH	−2.61	19.30	<0.001	0.07	0.02–0.23
APACHE-II Score	0.38	18.55	<0.001	1.46	1.23–1.74
SOFA Score	0.77	17.09	<0.001	2.17	1.50–3.13
Charlson Score	0.76	7.41	<0.001	2.14	1.23–3.70
Total number of medication	0.12	0.69	0.40	1.12	0.84–1.49
Total number of medication with supplements	0.00	0.00	0.95	1.00	1.77–1.30

11. Risk factors for delirium

Many studies have evaluated the risk factors for delirium in patients undergoing cardiac surgery. In a recent review, Koster et al [30,31] reviewed the data for risk factors leading to the development of delirium in patients undergoing cardiac surgery and identified 27 risk factors — 12 predisposing and 15 precipitating factors for delirium after cardiac surgery. Among the various risk factors, certain risk factors like increased age, pre-existing cognitive impairment, severe co-existing illnesses, and exposure to medication are considered as robust risk factors [32]. Another review of data for risk factors associated with development of delirium in patients undergoing cardiac surgery identified 33 risk factors: 17 predisposing and 16 precipitating factors for delirium after elective cardiac surgery. The common predisposing risk factors were age, depression, history of stroke, cognitive impairment, diabetes mellitus and atrial fibrillation. The precipitating risk factors and variables associated with delirium were duration of surgery, prolonged intubation, surgery type, red blood cell transfusion, elevation of inflammatory markers and plasma cortisol level and postoperative complications [33].

When one closely looks at the findings of the present study and compares it with literature from other countries, which is mostly from the Western countries, it emerges that there are certain factors which are common to development of delirium, irrespective of the country, and these factors includes older age, higher number of medications, higher severity of physical illness and presence of comorbidity. However, certain other factors like type of metabolic disturbance, sepsis, etc., vary from study to study and possibly influence the incidence and prevalence of delirium. Considering the fact that there are certain risk factors for delirium which can be modified, the clinician dealing with cardiac ICU patients must be made aware of these risk factors, so as to cut down on the possibly avoidable risk factor and overall incidence and prevalence of delirium. Further, if these cannot be avoided then the clinician should be vigilant for emergence of delirium and manage it appropriately.

12. Outcome of subjects with delirium:

Higher mortality rate in patients with delirium supports the existing vast literature which suggests that delirium leads to higher mortality irrespective of the study setting [12,34–36]. With respect to predictors of mortality presence of uncontrolled diabetes mellitus, cardiogenic shock and sepsis had highest odds ratio for predicting in hospital mortality. Other predictors of mortality in the hospital were presence of diabetes mellitus, higher APACHE-II score, higher SOFA score and higher Charlson Comorbidity Index score. Findings of the present study also suggest that delirium leads to prolonged ICU stay and supports the earlier findings [12].

Findings of the present study must be interpreted in the light of the limitations of our study. The present study was restricted to a single cardiac ICU. In the present study, long-term outcome in the form of cognitive deficits as a result of delirium and mortality were not assessed. Different factors associated with cardiac interventions (duration of intervention, blood loss, complications, etc.) were not evaluated as the predictors of delirium.

To conclude this prospective study with daily assessment was able to identify cases of delirium in patients with cardiac illnesses admitted to cardiac ICU. This study shows that about one-fourth of patients admitted to cardiac ICU develop delirium. Further this study shows that there are many predictors of delirium, some of which can be easily modified. The present study also supports the notion that delirium is associated with high mortality and prolonged ICU stay. Hence, it is important that clinicians working in the cardiac ICU set-up must be made aware of the incidence and prevalence of delirium and must be alerted to modify the reversible predictors of delirium to reduce the mortality of these patients.

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