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The evaluation of frequency and predictors of delirium and its short-term and long-term outcomes in hospitalized older adults'

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ABSTRACT

Background: Delirium is a common complication in hospitalized older adults with multifactorial etiology and poor health outcomes.
Aim: To determine the frequency and predictors of delirium and its short-term and long-term outcomes in hospitalized older adults.
Methods: A prospective observational study was performed in patients aged ≥60 years consecutively admitted to geriatric ward. Potential risk factors were assessed within 24 hours of hospital admission. Delirium screening was performed on admission and daily thereafter throughout the hospital stay using Confusion Assessment Method (CAM). Patients were followed up at 1-year post-discharge.
Results: The study included 200 patients with mean age 73.1 ± 8.83 years. Incidence and prevalence rate of delirium were 5% and 20% respectively. Multivariable regression analysis revealed emergency admission (OR= 5.12 (1.94–13.57), p=0.001), functional dependency (Katz index of Independence in Activities of Daily Living (Katz-ADL) score <5) 2 weeks before admission (OR= 3.08 (1.30–7.33), p=0.011) and more psychopathological symptoms (higher Brief Psychiatric Rating Scale (BPRS) total score) (OR=1.12 (1.06–1.18), p=0.001) to be independently associated with delirium. Patients in delirium group had significantly high in-hospital mortality (OR= 5.02 (2.12–11.8), p=0.001) and post-discharge mortality (HR= 2.02 (1.13–3.61), p=0.017) and functional dependency (Katz-ADL score <5) (OR= 5.45 (1.49–19.31), p=0.01) at 1-year follow up.
Conclusion: Delirium is quite frequent in geriatric inpatients and is associated with high in-hospital and post-discharge mortality risk and long-term functional dependency. Emergency admission, pre-hospitalization functional dependency, and more general psychopathological symptoms are independently associated factors. Hence, earliest identification and treatment with early implementation of rehabilitation services is warranted.

1. Introduction

The term 'Delirium' is currently conceptualized as a complex, reversible neuropsychiatric disorder with an acute onset and fluctuating course. It is typically characterized by disturbances in attention and cognitive domains (memory, orientation, language, visuospatial ability or perception) with or without alteration in non-cognitive domains such as sleep wake cycle and thought process (Harrington and Vardi, 2013). It can be divided into three motoric subtypes: hypoactive, hyperactive and mixed (Hshieh et al., 2020).

By virtue of socioeconomic development, the world is seeing a rapid transition in demographics with proportion of older people rising

Abbreviations: CAM, Confusion Assessment Method; CCI, Age-Adjusted Charlson Comorbidity Index; CI, Confidence Interval; DHS, Duration of hospital stay; DRS-R98, Delirium Rating Scale-Revised version; HDU, High Dependency Unit; HR, Hazards ratio; ICU, Intensive Care Unit; IQCODE-SF, The Informant Questionnaire on Cognitive Decline in the Elderly-Short Form; BPRS, Brief Psychiatric Rating Scale; Katz-ADL, Katz index of Independence in Activities of Daily Living; Max, Maximum; Min, Minimum; NLR, Neutrophil-Lymphocyte Ratio; OPD, Outpatient department; OR, Odds Ratio; RASS, Richmond Agitation and Sedation Scale; SD, Standard Deviation.

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precipitously. In India, people aged ≥60 years are projected to rise from 8.6% in 2011 to 19% by the year 2050 (Subaiya and Bansod, 2014). Despite being the most common complication affecting hospitalized older adults with risk increasing from 3% in <65 years to 14% in 65–74 years to 36% in ≥ 75 years, it largely remains under recognized, poorly understood and inadequately managed (Pendlebury et al., 2015)

In older persons, it has a multifactorial etiology involving a complex interrelationship between various predisposing factors such as advanced age, male gender, illiteracy, unemployment, living status, major and mild neurocognitive disorders, functional impairment, comorbidity burden, polypharmacy; and precipitating factors such as infection, central nervous system insults (e.g. stroke, meningitis), cardiac insults (like acute myocardial infarction, heart failure), treatment in intensive care unit (ICU), prolonged hospitalization, trauma or urgent admission and physiological insults like electrolyte disturbances, uraemia or hypoalbuminemia (Harrington and Vardi, 2013; Hshieh et al., 2020; Oldroyd et al., 2017; Banerdt et al., 2021).

Although previous studies conducted in adult patients in critical care settings have shown association of delirium with short-term outcomes like increased in-hospital mortality, longer duration of hospital stay, and long-term outcomes such as cognitive decline, however, results have been inconsistent with regards to association with post discharge mortality and very few studies have determined association with long-term functional decline in general medical settings (Pendlebury et al., 2015; Salluh et al., 2015; Altman et al., 2018; Hughes et al., 2021).

The presence of psychopathological symptoms and possible psychiatric morbidity have been established in surgical patients after delirium occurrence, however, no available evidence till date has evaluated their role as predictor of delirium in geriatric inpatients (Schneider et al., 2002; Langan et al., 2017).

With paucity of evidence in older adults admitted in geriatric wards, the need for this study surfaced to develop strategies and tools to identify those at maximum risk in geriatric medical wards, offering potential targets of intervention and helping clinicians prognosticate about potential complications and outcomes (Salluh et al., 2015; Billig et al., 2022; Grover et al., 2021). This study aims to evaluate the frequency rates of delirium, its sociodemographic, clinical and biochemical predictors and determine its short-term and long-term outcomes in patients aged 60 years and above admitted to geriatric ward of a tertiary care hospital.

2. Materials and methods

2.1. Sample size

Based on extensive literature review, prevalence of delirium in older adults varies from 11% to 42% in medical wards (Kukreja et al., 2015). We considered 42% prevalence of delirium with absolute error of 7% and at 95% confidence level. The required sample size was found to be 200 subjects. An adequate sample size for regression analysis to determine the risk factors should always be 10 times the amount of the factors/variables in analysis.(Pavlou et al., 2015). Therefore, this sample size was considered to be adequate to analyse 20 risk factors.

2.2. Study design

A prospective observational study was conducted between July 1, 2019 and October 31, 2020 after obtaining the ethical clearance from the institute's ethical committee (Reference no.: IECPG-34/23.01.2019). The study included patients aged 60 years and above consecutively admitted under Department of Geriatric medicine after seeking written informed consent from the patient or immediate caregiver of the patient at the time of admission. The patients recruitment was held from July 1, 2019 to October 31, 2019. Patients who withdrew consent, had duration of hospital stay less than 24 hours, history of psychiatric illness or admitted for alcohol withdrawal delirium were excluded from the study. The admitted patients were provided a multidisciplinary care approach with team comprising of geriatricians, nurses, physiotherapist, dieticians and psychologists. Patients discharged from hospital were followed up at 1-year from the time of discharge using telephonic interviews to determine current status (dead or alive; time of death noted in months from discharge) and functionality status using Katz-ADL score. Flowchart of participant inclusion is depicted in Fig. 1.

2.3. Baseline assessment

Patients were assessed for delirium within 24 hours of admission and daily thereafter throughout their hospital stay, till the time of discharge or death whichever was earlier, using Confusion Assessment Method (CAM) or CAM-ICU scale. These tools have been widely used, extensively validated and have high interrater reliability with CAM having sensitivity of 94%-100% and specificity of 90%-95% (Hshieh et al., 2020) and CAM-ICU having sensitivity of 80% and specificity of 96% (Rieck et al., 2020).

Following data was collected at the time of admission using clinical questionnaires and assessment tools:

a) Sociodemographic: Age, sex, education, employment and living status;
b) Clinical: Mode of admission (Outpatient department (OPD) or emergency); admission in High Dependency Unit (HDU)/ICU; comorbidity burden by Age-Adjusted Charlson Comorbidity Index (CCI) (Charlson et al., 1994); polypharmacy (defined as the use of ≥ 5 medications); level of functional impairment by Katz index of Independence in Activities of Daily Living (Katz-ADL) (Katz et al., 1970) at the time of admission and 2 weeks before admission with a score < 5 depicting functional dependence and ≥ 5 reflecting functional independence; level of cognitive decline by The Informant Questionnaire on Cognitive Decline in the Elderly-Short Form (IQCODE-SF) (Jorm, 1994) which includes 16 items and requires caregivers to rate changes in older patient's cognitive performance over previous 10 years on a 5 point Likert scale. A cut off score <3.00 indicates improvement, 3.00 no change, 3.01–3.50 slight decline, 3.51–4.00 moderate decline, and 4.01–5.00 severe decline; psychopathological symptomatology by Brief Psychiatric Rating Scale (BPRS) (Overall and Beller, 1984) which consists of 18 symptom constructs such as hostility, suspiciousness, hallucination, and grandiosity with each item scored on a 7-point scale from 1 (not present) to 7 (extremely severe). All the items that cannot be assessed are rated 0; type of delirium by Richmond Agitation and Sedation Scale (RASS) with score −1 to −3 indicating hypoactive, +1 to +4 indicating hyperactive and alternating subtypes indicating mixed type (Sessler et al., 2002); cause of delirium; severity and phenomenology of delirium by Delirium Rating Scale–Revised version-severity score (DRS-R98-severity) which consists of 13 item symptom construct (Trzepacz et al., 2001);
c) Biochemical: Complete blood count (including Hemoglobin and Neutrophil-Lymphocyte Ratio (NLR), albumin levels and kidney function test with serum electrolytes. For this, a total of 2 ml of venous blood was collected from each patient under aseptic conditions and sent to hospital laboratory as per the standard procedure.

2.4. Outcome

Patients who did not have delirium at baseline (within 24 hours of admission) but were diagnosed with delirium in subsequent days were classified as new cases and were counted towards 'incidence' rate. Whereas all the patients found to have delirium at any stage of their hospital stay (i.e. within 24 hours of admission or developing delirium after that) were counted as total cases and constituted the 'prevalence' rate. The study's initial end point was discharge from the hospital or

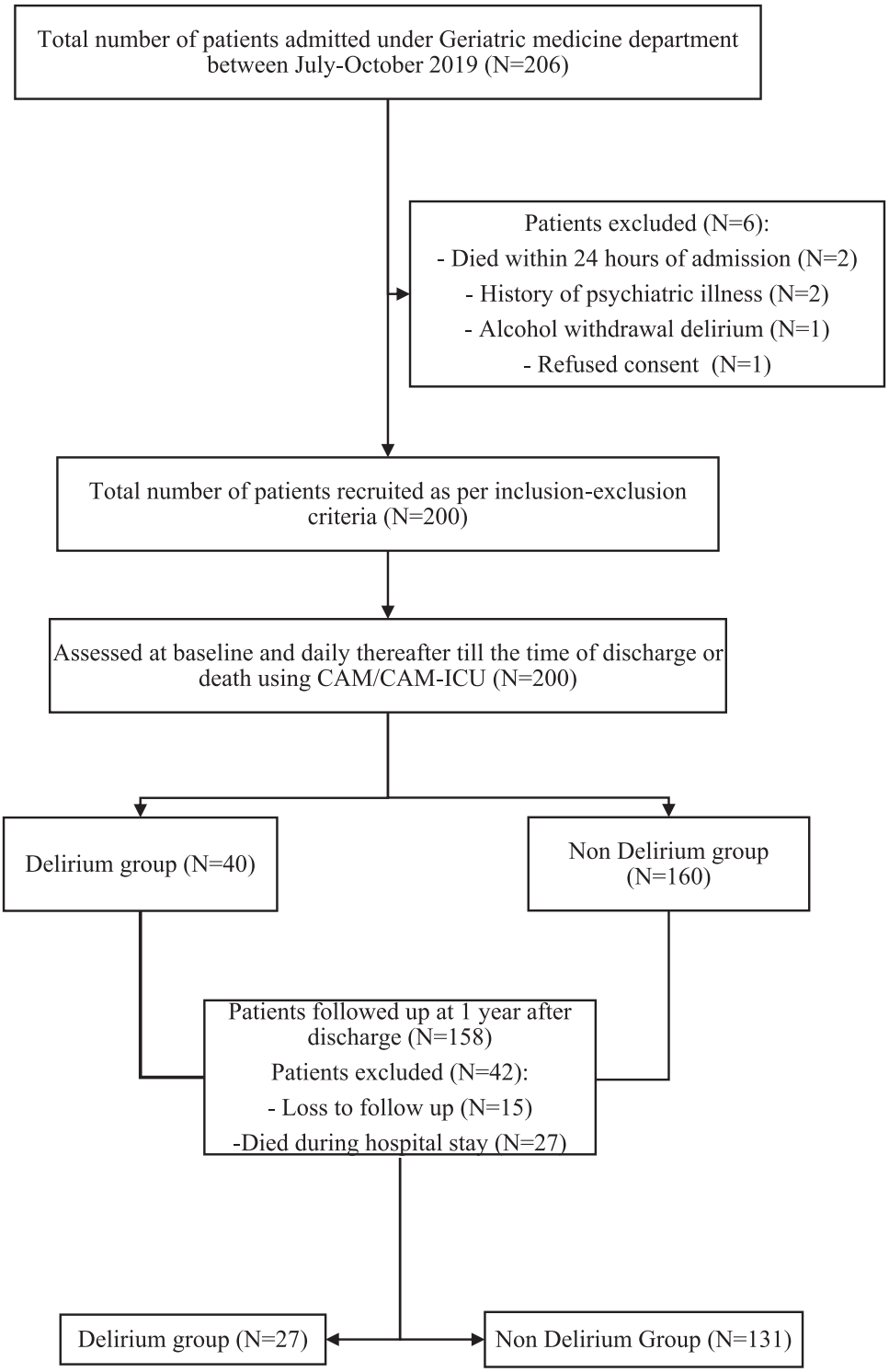

Fig. 1. Flowchart of participant inclusion in the study.

death whichever was earlier and final end point was functionality status and mortality status at 1-year follow up period.

2.5. Statistical analysis

It was done using STATA 16.0 (StataCorp, College Station, TX) software. Initially, descriptive statistics was used to analyse the data. For qualitative variables, absolute frequency and related percentage distribution and for quantitative variables, mean and standard deviation (SD) for normally distributed and median (minimum-maximum) for non-normally distributed variables were reported. Firstly, to establish the association, Pearson chi-square test/ Fisher exact test were applied for categorical variables and independent t-test/ Wilcoxon rank sum test were applied for quantitative variables. Delirium regression models were performed based on prevalence variable. Associations between delirium and its risk factors were estimated by odds ratio (OR) and their corresponding 95% confidence interval (CI) using univariable logistic regression analysis. For selection of variables for multivariable analysis,

a stepwise selection procedure using entry criteria of 0.15 and exit criteria of 0.05 based on univariable analysis, along with inclusion of sex as an independent variable in analysis. For assessing the outcome at 1 year, initially Pearson chi-square test and Wilcoxon rank sum test were used to establish association with mortality and functional impairment respectively. Kaplan-Meier survival estimates with 95% confidence interval were plotted for both delirium and non-delirium group. Cox regression analysis was performed to estimate Hazard ratio (HR) and their 95% confidence interval to compare survival between both the groups. The diagnostic assumptions of the cox regression model, proportional hazards assumption, examination of influential observations (or outliers) and detecting non linearity in relationship between the log hazard and the covariates were examined using Residuals method. Initially, univariable cox regression analysis was performed to determine effect of baseline covariates individually on survival. A stepwise selection procedure, using entry probability of 0.10 and exit probability of 0.05 was used to select variables for multivariable cox regression analysis. Logistic regression analysis was performed to establish association with functional impairment between 2 groups at 1-year follow up.

All p-values were 2 tailed and statistical significance was considered at < 0.05.

3. Results

The mean age of study sample was 73.1 ± 8.8 years. 30 out of 200 patients were found to have delirium at baseline (within 24 hours of admission) whereas 10 out of 200 patients developed delirium in subsequent days during hospital stay giving us an incident rate of 5% and prevalence rate of 20%. Hypertension (56.5%) and Type 2 Diabetes Mellitus (38%) were the most common diseases identified. The sociodemographic, clinical and biochemical characteristics of study participants are presented in Table 1.

In terms of psychopathological symptomatology, delirium patients had significantly less somatic concern, anxiety, grandiosity, and significantly more emotional withdrawal, conceptual disorganization, mannerisms and posturing, hallucinatory behavior, blunted affect, excitement and disorientation ($p<0.01$). (Table 1)

The median duration of delirium was 5 days. Hypoactive delirium was the commonest subtype (77.5%) and sepsis (50%) was the commonest aetiology. As per phenomenology, 100% patients had disturbances in sleep wake cycle, orientation, attention and long-term memory followed by 97.5% patients having short-term memory disturbances (Table 2).

3.1. Potential risk factors for delirium

Univariable analysis revealed significant increase in odds of having delirium with rising age, emergency admission, ICU/HDU admission, higher IQCODE-SF score, higher BPRS score, high NLR and sodium levels, Katz-ADL score <5 (dependent) 2 weeks before admission, and lower albumin levels ($p<0.05$). Emergency admission ($p=0.001$), Katz-ADL score <5 2 weeks before admission ($p=0.011$) and higher BPRS total score ($p=0.001$) remained independently associated with delirium in multivariable analysis (Table 3).

3.2. Short-term outcome of delirium

Having delirium significantly increased the odds of having in-hospital mortality by 5 times (OR=5.02, 95% CI 2.12–11.8, $p=0.001$) (Table 3).

3.3. Long term outcomes of delirium (at 1-year follow up)

At 1-year follow up, significant increase in death was reported in delirium group in comparison to non-delirium group (15/27 (55.5%) vs

Table 1
Sociodemographic, clinical and biochemical characteristics of study participants.

Variables	Description (n (%) / Mean ± SD/ Median (Min/max)			
	Total (N=200)	Non Delirium Group (N=160)	Delirium group (N=40)	p value
Age (in years)	73.1 ± 8.8	72.2 ± 8.5	76.4 ± 9.5	0.007**
60–69 years	79 (39.5%)	68 (42.5%)	11 (27.5%)	.
70–79 years	68 (34%)	54 (33.7%)	14 (35%)	.
80–89 years	48 (24%)	36 (22.5%)	12 (30%)	.
>90 years	5 (2.5%)	2 (1.2%)	3 (7.5%)	.
Sex	.	.	.	0.393
Male	112 (56%)	92 (57.5%)	20 (50%)	.
Female	88 (44%)	68 (42.5%)	20 (50%)	.
Education	.	.	.	0.718
Illiterate	62 (31%)	50 (31.2%)	12 (30%)	.
≤ High school	83 (41.5%)	68 (42.5%)	15 (37.5%)	.
>High school	55 (27.5%)	42 (26.3%)	13 (32.5%)	.
Occupation	.	.	.	0.615
Employed	82 (41%)	67 (41.8%)	15 (37.5%)	.
Unemployed	118 (59%)	93 (58.1%)	25 (62.5%)	.
Living status	.	.	.	0.585
With family	195 (97.5%)	155 (96.8%)	40 (100%)	.
Alone	5 (2.5%)	5 (3.1%)	0 (0%)	.
Mode of admission	.	.	.	0.001**
OPD	134 (67%)	118 (73.7%)	16 (40%)	.
Emergency	66 (33%)	42 (26.2%)	24 (60%)	.
ICU/HDU admission	52 (26%)	24 (15%)	28 (70%)	0.001**
CCI	6 (2–15)	6 (2–15)	6 (3–15)	0.98
Polypharmacy	98 (49%)	81 (50.6%)	17 (42.5%)	0.358
Katz-ADL < 5	.	.	.	.
2 weeks before admission				0.001**
Yes (Dependent)	70 (35%)	47 (29.4%)	23 (57.5%)	
No (Independent)	130 (65%)	113 (70.6%)	17 (42.5%)	
On admission				0.001**
Yes (Dependent)	141 (70.5%)	101 (63.1%)	40 (100%)	
No (Independent)	59 (29.5%)	59 (36.9%)	0 (0%)	
IQCODE-SF score	3.4 ± 0.5	3.3 ± 0.4	3.6 ± 0.7	0.002**
Level of Cognitive Decline	.	.	.	0.018*
Improvement	0 (0%)	0 (0%)	0 (0%)	.
No change	21 (10.5%)	20 (12.5%)	1 (2.5%)	.
Mild decline	130 (65%)	107 (66.9%)	23 (57.5%)	.
Moderate decline	30 (15%)	22 (13.7%)	8 (20%)	.
Severe decline	19 (9.5%)	11 (6.9%)	8 (20%)	.
BPRS total score	36.2 ± 8.5	34.8 ± 8.1	41.8 ± 7.9	0.001**
Somatic concern	3.5 ± 1.7	3.8 ± 1.5	2.5 ±1.9	0.001**
Anxiety	3.3 ± 1.7	3.4 ± 1.6	2.5 ± 1.9	0.002**
Emotional withdrawal	2.6 ± 1.7	2.3 ±1.6	3.7 ± 1.9	0.001**
Conceptual disorganization	1.6 ± 1.3	1.3 ± 0.9	2.6 ± 2.0	0.001**
Guilt feelings	1.6 ± 1.3	1.6 ± 1.3	1.4 ± 1.4	0.313
Tension	1.6 ± 1.2	1.6 ± 1.2	1.6 ± 1.2	0.881
Mannerisms and posturing	1.5 ± 1.1	1.4 ± 1	2.0 ± 1.5	0.002**
Grandiosity	1.0 ± 0.54	1.1 ± 0.6	0.8 ± 0.4	0.003**
Depressive mood	3.1 ± 1.6	3.1 ± 1.6	3.0 ± 1.6	0.875
Hostility	1.2 ± 0.9	1.2 ± 0.8	1.4 ± 1.2	0.354
Suspiciousness	1.1 ± 0.8	1.1 ± 0.8	1.2 ± 1.1	0.431
Hallucinatory behavior	1.1 ± 0.7	1.1 ± 0.6	1.3 ± 0.9	0.022*
Motor retardation	4.1 ± 1.5	4.0 ± 1.4	4.4 ± 1.7	0.141
Uncooperativeness	1.6 ± 1.2	1.6 ± 1.1	1.8 ± 1.4	0.261
Unusual thought content	1.0 ± 0.5	1 ± 0.3	1.1 ± 0.8	0.128
Blunted affect	2.8 ± 1.7	2.4 ± 1.5	4.2 ± 1.6	0.001**
Excitement	1.2 ± 0.7	1.1 ± 0.5	1.5 ± 1.2	0.002**
Disorientation	1.2 ± 1.9	1.3 ± 1.2	4.5 ± 1.9	0.001**
Hemoglobin (g/dL)	10.3 ± 2.4	10.3 ± 2.5	10.7 ± 1.9	0.34
NLR	5.4 (0.1–92.6)	4.8 (0.1–74)	7.3 (1.2–92.6)	0.003**

(continued on next page)

Table 1 (*continued*)

Variables	Description (n (%) / Mean ± SD/ Median (Min/max)			
	Total (N=200)	Non Delirium Group (N=160)	Delirium group (N=40)	p value
Urea (mg/dL)	42 (8–374)	37 (8–374)	51 (16–341)	0.02*
Creatinine (mg/dL)	1 (0.3–17.2)	1 (0.3–14.7)	1 (0.4–17.2)	0.92
Calcium (mg/dL)	8.1 ± 1.3	8.2 ± 1.3	8.0 ± 1.3	0.47
Sodium (mEq/L)	137.9 ± 7.3	137.4 ± 6.9	140.2 ± 8.5	0.03*
Potassium (mEq/L)	4.3 ± 0.7	4.3 ± 0.7	4.3 ± 0.8	0.81
Albumin (g/dL)	3.1 ± 0.7	3.2 ± 0.7	2.9 ± 0.6	0.026*
DHS (in days)	8.5 (2–39)	8.2 (2–39)	10.5 (2–30)	0.07
Outcome	.	.	.	0.001**
Discharge	173 (86.5%)	146 (91.2%)	27 (67.5%)	.
Death	27 (13.5%)	14 (8.7%)	13 (32.5%)	.

* level of significance <0.05,
** level of significance <0.01; Abbreviations: SD: Standard deviation; Min: Minimum; Max: Maximum; OPD: Outpatient department; ICU: Intensive Care Unit; HDU: High Dependency Unit; CCI: Age-Adjusted Charlson Comorbidity Index; Katz-ADL: Katz index of Independence in Activities of Daily Living; IQCODE-SF: The Informant Questionnaire on Cognitive Decline in the Elderly-Short Form; BPRS: Brief Psychiatric Rating Scale; NLR: Neutrophil-Lymphocyte ratio; DHS: Duration of hospital stay;

Table 2
Clinical characteristics of patients with delirium.

Variables	n (%)
Type of Delirium	.
Hyperactive	8 (20%)
Hypoactive	31 (77.5%)
Mixed	1 (2.5%)
Cause of delirium	.
Sepsis	20 (50%)
Electrolyte imbalance	5 (12.5%)
Intracranial pathologies (including stroke, tubercular meningitis, autoimmune encephalitis)	8 (20%)
Miscellaneous (including post- operative, idiopathic, pain, poisoning, heart failure)	7 (17.5%)
Duration of delirium (in days), median (IQR)	5 (3–9)
DRS-R98-severity, mean ± SD	19.5 ± 5.2
Sleep-wake cycle disturbance	40 (100%)
Perceptual disturbance and hallucinations	8 (20%)
Delusions	3 (7.5%)
Lability of affect	24 (60%)
Language, n (%)	22 (55%)
Thought process abnormalities	32 (80%)
Motor agitation	9 (22.5%)
Motor retardation	31 (77.5%)
Orientation	40 (100%)
Attention	40 (100%)
Short-term memory	39 (97.5%)
Long-term memory	40 (100%)
Visuospatial inability	29 (72.5%)

Abbreviations: IQR: Interquartile range; DRS-R98: Delirium Rating Scale-Revised version; SD: Standard deviation;

49/131 (37.4%), p=0.08). The Kaplan-Meier curve showed significant decrease in survival of patients in delirium group throughout the follow up period (Log-Rank test, p=0.028). The widened confidence interval in delirium group relays to lesser number of patients in that group (Fig. 2). Univariable cox regression analysis revealed strong association of delirium with 1-year mortality (HR= 1.86, 95% CI 1.04–3.39, p=0.035). Multivariable analysis showed mortality risk to increase by two folds in

Table 3
Factors associated with delirium.

Variable	Univariable analysis		Multivariable analysis	
	Odds Ratio (95% CI)	p value	Odds Ratio (95% CI)	p value
Age	1.05 (1.01–1.09)	0.007**	1.04 (0.99–1.09	0.11
Female Sex	1.35 (0.67–2.70)	0.394		
Emergency admission	4.21 (2.04–8.69)	0.001**	5.12 (1.94–13.57)	0.001**
ICU/HDU admission	13.22 (5.92–29.5)	0.001**		
Polypharmacy	0.72 (0.35–1.45)	0.357		
Katz-ADL <5 (Dependent)	.	.		
2 weeks before admission	3.25 (1.59–6.64)	0.001**	3.08 (1.30–7.33)	0.011*
On admission	1			
IQCODE-SF score	2.44 (1.32–4.49)	0.005**		
CCI	1.01 (0.89–1.15)	0.78		
BPRS total score	1.10 (1.05–1.15)	0.001**	1.12 (1.06–1.18)	0.001**
DHS (in days)	1.04 (0.99–1.10)	0.056		
Outcome, death	5.02 (2.12–11.8)	0.001**		
Hemoglobin (g/dL)	1.07 (0.92–1.23)	0.339		
NLR	1.03 (1.01–1.05)	0.008**	1.02 (0.99–1.05)	0.10
Urea (mg/dL)	1.00 (0.99–1.01)	0.199		
Creatinine (mg/dL)	1.06 (0.92–1.23)	0.415		
Calcium (mg/dL)	0.91 (0.70–1.17)	0.488		
Sodium (mEq/L)	1.05 (1.0–1.1)	0.033*		
Albumin (g/dL)	0.56 (0.33–0.93)	0.025*		

* level of significance <0.05,
** level of significance < 0.01; Abbreviations: CI: Confidence Interval; ICU: Intensive Care Unit; HDU: High Dependency Unit; Katz-ADL: Katz index of Independence in Activities of Daily Living; IQCODE-SF: The Informant Questionnaire on Cognitive Decline in the Elderly-Short Form; CCI: Age-Adjusted Charlson Comorbidity Index; BPRS: Brief Psychiatric Rating Scale; DHS: Duration of hospital stay; NLR: Neutrophil-Lymphocyte ratio;

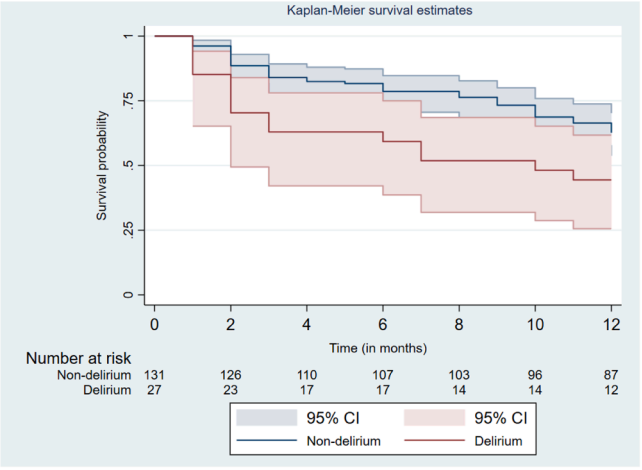

Fig. 2. Kaplan-Meier survival estimates showing significant decrease in survival rates of patients in delirium group as compared to non-delirium group up to 1-year follow up (Log-Rank test, p=0.028); CI: Confidence Interval.

delirium group (HR= 2.02, 95% CI 1.13–3.61, p=0.017). It also showed independent association of high comorbidity burden (via CCI) with high mortality risk and female sex with low mortality risk (Table 4).

At 1-year follow up, significantly higher number of patients were found to be functionally dependent (Katz-ADL score <5) in delirium group compared to those in non-delirium group (66.7% vs 26.8%, p=0.006). Subsequently, logistic regression analysis revealed 5 folds increase in odds of having functional dependency (Katz-ADL score <5) in delirium group (OR= 5.45, 95% CI 1.49–19.31, p=0.01).

4. Discussion

This study determined the frequency and sociodemographic, clinical and biochemical predictors of delirium and evaluated its short-term and long-term outcome in hospitalized older adults. The prevalence and incidence rates of delirium i.e. 20% and 5% respectively are in accordance with some of the previous studies reporting prevalence and incidence rates to be 11–42% and 6–56% respectively (Kukreja et al., 2015; Garcez et al., 2019; Kim et al., 2018; Zhang et al., 2022); But lower from those studies which found prevalence and incident rates to be 25–57% and 20–29% respectively in old age medicine wards (Hshieh et al., 2020; Grover et al., 2021; Weng et al., 2019). The possible explanation for lower incidence rates could be application of targeted multicomponent nonpharmacologic interventions in geriatric ward like providing bed rails, corridor rails, grab bars in toilets, pain management, encouraging regular visits from family and friends, promoting early mobilization and regular ambulation, giving orientation clues, avoiding physical restraints and medical/nursing procedures during sleep which primarily help in restoration of normal circadian rhythm. A recent literature review showed circadian rhythm disturbances to be an integral factor in addition to other essential criteria while diagnosing delirium (Mukku et al., 2023).

Hypoactive delirium was the commonest subtype (77.5%) followed by hyperactive and mixed type. Findings are similar to recent systematic review (Grover et al., 2021; Krewulak et al., 2018); However, a recent study reported mixed type (66%) as the commonest subtype (Simons et al., 2018). In the current study, as patients were being assessed for delirium once daily, therefore, the possibility of mischaracterization of some cases as hypoactive type instead of mixed type cannot be ruled out. A recent bibliometric analysis on delirium subtype research showed an exponential growth trend (from 2010 to 2023) in the number of publications on delirium subtypes with availability of several subtype instruments, however, very few publications have reported the consistency of results regarding delirium subtypes, therefore which is the most suitable instrument to assess subtype remains unclear. (Zhou et al., 2023)

Sepsis (50%) was found to be most common aetiology, followed by intracranial pathologies (20%) and electrolyte disturbances (12.5%). In difference to previous studies, an increase in frequency of intracranial pathologies could be due to ready availability and advancement in brain imaging and invasive techniques like CSF analysis in the past decade; and decrease in electrolyte disturbances may be because of availability of routine blood tests leading to early identification and management (Khurana et al., 2011; Magny et al., 2018).

According to available literature, although duration of delirium may vary from few hours to months (maximum 6 months), it mostly resolves within 1–2 weeks. The decreased duration in current study (5 days) is in line with previous review which attributed early diagnosis and multidisciplinary care given in specialized geriatric unit to result in absolute risk reduction of delirium by 20% and decrease in average duration by 5 days (Iglseder et al., 2022).

As per phenomenology, almost all patients were found to have disturbances in sleep wake cycle, orientation, attention, long term and short term memory. The findings re-establishes cognition and attention as the core elements of delirium (Grover et al., 2021; Glynn et al., 2021).

The findings of regression analysis showing older age, emergency admissions, ICU/HDU admission and cognitive decline as associated factors of delirium adds to the available literature (Oldroyd et al., 2017; Billig et al., 2022; Zhang et al., 2022; Ahmed et al., 2014; Rieck et al., 2020). The study shows functional dependency (Katz-ADL score <5) 2 weeks before admission to have independent association with delirium and 100% patients in delirium group were found to be functionally dependent at the time of admission. This finding of association of pre-hospitalization functionality with delirium adds remarkably to the available literature which reports delirium association of functional impairment mainly after hospitalization (Mosk et al., 2017; Rieck et al., 2020; Ahmed et al., 2014; Korevaar et al., 2005).

Among the biochemical markers, analysis revealed significant association of delirium with high levels of NLR and low levels of albumin. NLR, a known marker of inflammation and oxidative stress, has been found to play a role in neuroinflammatory hypothesis of delirium, can be easily derived from circulation, and hence might serve as a potential biomarker of delirium in future (Egberts and Mattace Raso, 2017; Zhao et al., 2021).

The study results re-establishes significant association of delirium with short-term outcomes such as in-hospital mortality which is in consistence with a recent meta-analysis. The higher mortality rates (32.5%) in current study further underlines the need for newer advances in the management of delirium (Grover et al., 2021; Aung Thein et al., 2020).

More general psychopathological symptoms, via BPRS tool, have been significantly associated with higher severity of delirium and prolonged duration in one study conducted in vascular surgical patients (Schneider et al., 2002). A recent systematic review concluded increased burden of psychiatric symptoms and possible psychiatric morbidity after delirium necessitating thorough assessment and potential treatment (Langan et al., 2017). The current findings of delirium patients having significantly less somatic concern, anxiety and grandiosity may be due to disorganized thinking; significantly more emotional withdrawal, blunted affect, conceptual disorganization and disorientation is probably due to cognitive disturbances in delirium and hypoactive delirium patients constituting more than 2/3rd cases; significantly more mannerisms and posturing, hallucinatory behavior and excitement highlights the presence of neuropsychiatric phenomenology in delirium patients.

The study results show significantly higher post discharge mortality risk at 1-year in patients diagnosed with delirium during hospital admission. These findings add remarkably to the literature as conflicting results exist regarding such association with a recent systematic review reporting no such association (Pendlebury et al., 2015; Salluh et al., 2015; Hughes et al., 2021). Patients in delirium group were also found to have significant long-term functional dependency. As very few studies have previously reported such association, these findings widen the

Table 4
Result of cox proportional hazard analysis of 1- year mortality.

	Univariable analysis		Multivariable analysis	
Variable	Hazard Ratio (95% CI)	p value	Hazard Ratio (95% CI)	p value
Delirium group	1.86 (1.04–3.39)	0.035*	2.02 (1.13–3.61)	0.017*
Age	1.01 (0.98–1.03)	0.384		
Female Sex	0.51 (0.30–0.87)	0.014*	0.53 (0.31–0.92)	0.025*
IQCODE-SF score	1.25 (0.78–2.00)	0.349		
CCI	1.12 (1.03–1.23)	0.007**	1.11 (1.01–1.21)	0.027*
BPRS total score	1.01 (0.99–1.04)	0.172		
DRS-R-98-severity score	1.03 (1.00–1.06)	0.036*		

* level of significance <0.05,
** level of significance <0.01; Abbreviations: CI: Confidence Interval; IQCODE-SF: The Informant Questionnaire on Cognitive Decline in the Elderly-Short Form; CCI: Age-Adjusted Charlson Comorbidity Index; BPRS: Brief Psychiatric Rating Scale; DRS-R98: Delirium Rating Scale-Revised version;

horizon of the available literature and infer that it is crucial to implement rehabilitation services early to reduce the risk of associated functional decline (Altman et al., 2018; Weng et al., 2019).

The study is strengthened by use of a prospective study design, extensively validated and reliable tools for assessment of clinical correlates and incorporation of consecutive sampling technique to prevent selection bias. Identification of delirium cases by a trained geriatrician prevented misdiagnosis or missed cases. This is a pioneer study in our knowledge that used BPRS as a tool to characterize psychopathological symptomatology in association with delirium in hospitalized older adults. This study also adds significantly to available literature by depicting significant association of delirium with post discharge mortality and functional dependency (at 1-year follow up). However, our study has some limitations. As cohort comprises of hospitalized inpatients aged 60 years and above, it limits the generalizability of results to community settings and younger population. The study does not capture the functional status of patients at any time point between discharge and 1-year, therefore occurrence of any illness or hospitalization during that time period affecting functionality status cannot be accounted for. Also, the design of the study precludes our ability to make causal inferences.

5. Conclusion

Delirium has high frequency of occurrence in geriatric inpatients and is independently associated with in-hospital and post-discharge mortality risk and long-term functional dependency. Therefore, it warrants early identification, better management practices and early implementation of rehabilitation services. A psychogeriatric evaluation approach with assessment of psychopathological symptoms along with assessment of functionality, both before hospitalization and at the time of admission, should be adopted at the time of admission to help establish those at risk. The multidisciplinary care approach provided in a geriatric unit may help reduce occurrence of incidence cases as well as decreased duration of delirium. However, acknowledging our study limitations, further large multicentric prospective studies are needed to confirm our results.

Ethical approval

The study was performed after obtaining approval from the Institute ethics committee, All India Institute of Medical Sciences, New Delhi (Reference no.: IECPG-34/23.01.2019) and is in line with the principles of the Declaration of Helsinki, 1964 (with amendments).

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CRediT authorship contribution statement

Karandeep Paul: Writing – review & editing, Writing – original draft, Conceptualization. **Maroof Ahmad Khan:** Writing – review & editing, Formal analysis. **Yamini Ajmera:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Aparajit Ballav Dey:** Writing – review & editing, Project administration, Conceptualization. **Avinash Chakrawarty:** Writing – review & editing, Writing – original draft, Project administration, Conceptualization. **Prasun Chatterjee:** Writing – review & editing, Conceptualization. **Bharti Kumari:** Writing – review & editing, Conceptualization. **Nand Kumar:** Writing – review & editing, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The datasets that support the findings of this study are available from the corresponding author upon reasonable request.

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Consent to participate

Written informed consent was obtained from participant or immediate caregiver of the patient for participating in the current study.

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