Original Article

Prevalence of Delirium in Advance Cancer Patients Admitted in Hospice Centre and Outcome after Palliative Intervention

Kikato V. Chishi[1], Bhavna Chirag Patel[1], Ravi A. Umrania[1], Priti Rashmin Sanghavi[1], Varun Shaileshbhai Yadav[1], Lekha V. Raval[1]

[1]Department of Palliative Medicine, Gujarat Cancer and Research Institute, Ahmedabad, Gujarat, India.

ABSTRACT

Objectives: The assessment of prevalence of delirium in advanced cancer patients admitted in hospice centre and outcome after palliative intervention. The possible related risk factors for development of delirium.

Material and Methods: This was prospective analytic study done at hospice centre attached with tertiary cancer hospital in Ahmedabad during August 2019 – July 2021. This study was approved by the Institutional Review Committee. We selected patients according to following inclusion criteria (all patient admitted to hospice centre above 18 years, with advance cancer disease and on best supportive care) and exclusion criteria (Lack of informed consent, Inability to participate in study due to mentally retard or coma). The following information were collected: age, gender, address, type of cancer, co-morbidities, history of substance abuse, history of (h/o) palliative chemotherapy or radiotherapy within last 3month, general condition, ESAS (Edmonton symptom assessment scale), ECOG (Eastern cooperative oncology group), PaP score (palliative prognostic score), medication including opioids, NSAIDs (Non-steroidal anti-inflammatory drugs), steroids, antibiotic, adjuvant analgesic, PPI (Proton pump inhibitor), anti-emetic etc. Delirium diagnosis was based on diagnostic criterion of DSM-IV text revised and MDAS.

Results: In our study we found prevalence of delirium was 31.29% in advanced cancer patients admitted to hospice centre. We found most common type of delirium is hypoactive (34.7%) and mixed subtype (34.7%) followed by hyperactive (30.4%) delirium. Resolution of delirium was higher among hyperactive delirium (78.57%) followed by mixed subtype (50%) and hypoactive (12.5%). Mortality was higher among patient with hypoactive subtype (81.25%) followed by mixed (43.75%) and hyperactive delirium (14.28%).

Conclusion: An identification and assessment of delirium is vital for acceptable end of life care within the palliative care in light of the fact that the presence of delirium is related with morbidity, mortality, prolonged ICU hospitalization, expanded time on a ventilator, and by and large more prominent medical services costs. Clinicians should utilize one of a few approved delirium assessment tools to help evaluate and archive cognitive function. Prevention and recognizing the clinical reason for delirium are generally the best method for diminishing the morbidity from delirium. The study results demonstrate that multi component delirium management or projects are generally proficient to lessen the prevalence and negative outcomes of delirium. It was found that palliative care intervention has quite a positive outcome as it not only focus on the mental health of the patients but also of family members who go through the same amount of distress and also help them to communicate properly and manage to settle the mental state and end the life without pain and distress.

Keywords: Delirium, Advanced cancer, Palliative care, Prevalence

INTRODUCTION

Delirium is a term derived from Latin word 'delirare' meaning to 'go out of furrow'. It is a common complex neuropsychiatric syndrome occurring in terminally ill-debilitated patients and those at end of life care. It also occurs with other conditions such as metabolic disturbances, dehydration, infection and head injuries. It is characterised by acute onset of disturbance in level of alertness, attention, perception, thinking, cognition, psychomotor behaviour, mood and sleep cycle. In terminal cancer patients, delirium prevalence can be as high as 85%.[1] Although reversibility can occur in one-third of cases with appropriate management, the survival among patients who develop delirium after admission is around 50%.[2] Occurrence of delirium is associated with significant morbidity, mortality, prolonged hospitalisation,

high cost and long-term consequence such as cognitive decline, impaired function and decrease quality of life.[3] Three clinical subtypes of delirium have been described based on psychomotor features and arousal level is hyperactive, hypoactive and mixed type.[4] High level of psychological distress has been reported by family caregivers and health-care provider due to potential irreversibility of condition and difficulty in assessing and managing patient needs.[5] Multiple risk factors for precipitating delirium include old age, terminal illness, acute illness, electrolyte disturbance, dehydration, drugs, metabolic disorder and therapeutic intervention like mechanical ventilation.[2] Although some cause of delirium in terminal cancer may be irreversible, yet, it is important in clinical practise to detect delirium and identify the reversible cause of delirium. Unfortunately, delirium is often missed and undertreated. Patients with delirium tend to present with symptoms exaggeration or less relief in comparison with the patient without delirium.[6] Hence, delirium screening is of most important in those patients who keep on experiencing worsening symptoms despite medical treatment. Delirium diagnosis was missed in more than 60% of patients by the primary referring team as revealed by palliative care consultation team.[7] Although health professionals acknowledge the importance for delirium screening in palliative care setting, actual implementation is not feasible due to lack of knowledge and confidence, unfamiliarity in using screening tool and unavailability of psychiatric services.[8] Various tools and criteria are available to help the clinician in diagnosing delirium including Delirium Rating scale,[9] Delirium Symptoms Interview,[10] Memorial Delirium Assessment Scale (MDAS),[11] and Diagnostic and Statistical Manual (DSM-IV)[12]. Standard management necessitates an examination of aetiology, treatment of contributing elements and symptomatic and steady treatments, involving various pharmacologic and non-pharmacological strategies for management of delirium assume a key part and ought to be upgraded through the aggregate endeavours of the entire inter professional group. Refractory agitated delirium somewhat in the last stage might need the utilisation of pharmacological sedation to alleviate patient's suffering.[13] Further, assessments of multi component strategies for prevention and treatment of delirium in palliative care patient populace are direly required. While data about prevalence of delirium are available in hospital, intensive care unit and acute palliative care set up, information regarding hospice are lacking. Hence, we did this study to find out prevalence of delirium in advanced cancer patients admitted at hospice and outcome after palliative intervention.

Aims and objectives

The objectives of this study were as follows:

1. The assessment of prevalence of delirium in advanced cancer patients admitted in hospice centre and outcome after palliative intervention

2. The possible related risk factors for development of delirium.

MATERIAL AND METHODS

This was prospective analytic study done at hospice centre attached with tertiary cancer hospital in Ahmedabad during August 2019–July 2021. This study was approved by the Institutional Review Committee. We selected patients according to following inclusion and exclusion criteria.

Inclusion criteria

All patients admitted to hospice centre above 18 years, with advance cancer disease and on best supportive care were included in the study.

Exclusion criteria

Lack of informed consent and inability to participate in study due to mentally retard or coma was excluded from the study. The following information were collected: Age, gender, address, type of cancer, comorbidities, history of substance abuse, history of (h/o) palliative chemotherapy (PCT) or radiotherapy (RT) within the past 3 month, general condition, Edmonton symptom assessment scale (ESAS), Eastern cooperative oncology group (ECOG), palliative prognostic score (PaP), medication including opioids, non-steroidal anti-inflammatory drugs (NSAIDs), steroids, antibiotic, adjuvant analgesic, Proton pump inhibitor, anti-emetic, etc.

Delirium diagnosis was based on diagnostic criterion of DSM-IV text revised[12] and MDAS.[11] DSM-IV consists of four criteria, in which all have to be fulfilled to make a diagnosis.[2,12]

i. Disturbance in consciousness (i.e., decreased clarity of environmental awareness) with decrease ability to focus, sustain and shift attention

ii. Change in cognition (disturbance in language, disorientation and memory deficit) or perception disturbances that are not better explained by a pre-existing established or evolving dementia

iii. The disturbance occurs over a short period (usually hours to days) and tends to fluctuate during the course of day

iv. There is evidence from history, physical examination or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition.

MDAS[11] consists of ten-item clinical rated scale for assessing delirium and its severity. Each item depending on its frequency and intensity is scored from 0 to 3 (possible range: 0–30). MDAS score of seven and above has been validated in advance cancer population. MDAS scale was used to screen the cognitive status of patients at time of admission and during the occurrence of delirium. It includes items on level of consciousness, short-term memory, disorientation,

digit span, disorganised thinking, attention, perceptual disturbance, psychomotor activity, delusion and sleep-wake cycle disturbance.

At admission, general data including primary tumour, age, gender, concomitant disease, general condition, ECOG performance status, symptoms assessment and PaP were collected. Possible risk factors for delirium were evaluated during admission. They include brain metastasis, fever, dehydration, substance abuse, palliative RT and CT in the past 3 months, cachexia, ECOG status and drugs such as opioids and antidepressant.

The ESAS[14] was used to assess the physical and psychological symptoms on admission. ESAS scale is used to measure the severity of ten different symptoms including pain, fatigue, nausea, appetite, drowsiness, breathlessness, anxiety, depression, sleep disturbance and well-being. It rates each symptom from 0 to 10, for example, Score 0 represent no pain and 10 representing worst possible pain.

ECOG[15] scale is the instrument to measure performance status. It grades the performance status of populace into five groups ranging from 0 to 5.

The PaP score[16] uses six criteria and includes dyspnoea, anorexia, white blood cell count; absolute lymphocyte count, clinical expected survival and karnofsky performance score, giving a score from 0 to 17.5. This score predicts three categorical risk for 30 days survival (A = 0–5.5; survival probability >70%, B = 5.6–11; survival probability 30–70%, C = 11.1–17.5 and survival probability <30%)

Palliative care intervention will include – Proper screening of potential aetiologies by taking detail history and physical examination, reviewing the medication list and laboratory investigation whenever indicated and treatment of causes.

Pharmacological management

Neuroleptic-haloperidol as first choice: Initial dose varying from 0.5 mg to 1 mg, orally or parenterally twice daily and titrate depending on age and severity of delirium. Benzodiazepines such as midazolam and lorazepam to control agitation if not control by neuroleptic. Other supportive measures such as rehydration with intravenous fluid, antibiotics and opioids switching and various symptoms management will be implement as need basis.

Non-pharmacological management

Multi-disciplinary team such as doctors, nurses, counsellor and dietician provides support and care to all patients and caregivers as per need basis. This consists of various measures such as providing comfort care; symptoms relief to promote sleep and rest; implementing various orienting measures such as providing clock, calendar; encouraging family visit to increase sense of familiarity and trust; using simple and clear instruction to facilitate understanding; providing appropriate environment such as room temperature and lighting; and monitor hydration and nutritional status.

Statistical analysis

In this study, the captured data from the quantitative research are presented and statistically analysed, described and interpreted in a systematic manner using Chi-square to evaluate the distributions of variables. Variables of $P < 0.005$ are taken as significant. Diagnosis of patients described in percentage. Variable of ESAS value of various symptoms and medication at time of admission is described in terms of mean, standard deviation and in percentage value.

RESULTS

One hundred and fifty patients admitted to hospice centre were screened in the time period taken into consideration. Three patients were not included in the study due to inability to communicate verbally due to disease associated loss of voice. Of 147 patients, 46 (31.29%) had delirium during their admission to hospice centre and 27 (18.367%) out of 147 had delirium at the time of admission. The median age was 50 year (20–95 years), as shown in Figure 1.

Figure 2 contains the list of primary cancer diagnosis. In our study population, head and neck cancer (57.8%) were the most common primary malignancy encountered, followed by breast cancer (10.2%) and lung cancer (7.5%).

Table 1 shows the ESAS value at the time of admission to hospice and the number of patients with ESAS score ≥7 signifying severe symptom. Pain (39.4%) was the most common severe symptom reported followed by decreased well-being (21%), sleep disturbance (19%) and fatigue (19%). Figure 3 shows current drug medication at the time of admission. Most common drugs were acetaminophen along with other NSAIDs (95.2%), followed by opioids (93.8%) commonly tramadol and morphine and H2 blocker-Ranitidine (72.2%).

Table 2 summarises the patient characteristics into two groups; those with delirium and those without delirium throughout the admission. Patients with poor ECOG
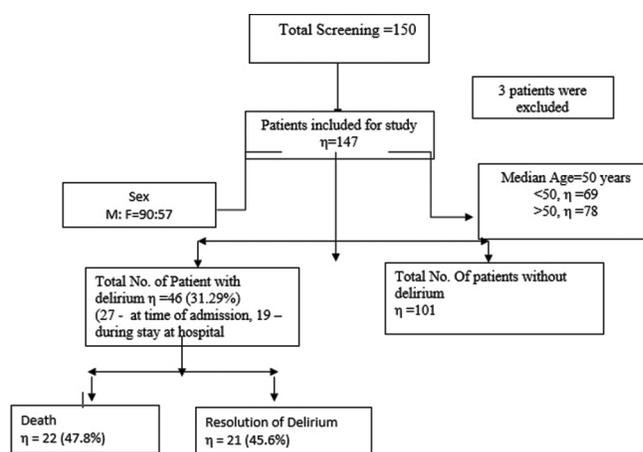

Figure 1: Distribution of patients admitted to the hospice centre with reference to the diagnosis of delirium.

performance status and poor prognostic PaP score were more likely to have diagnosis with delirium. No statistical significant difference in the two groups was found with regard with age, gender, palliative CT/RT taken in the past 3 month, or associated comorbidities. Statistically significant association was found with probable risk factors such as
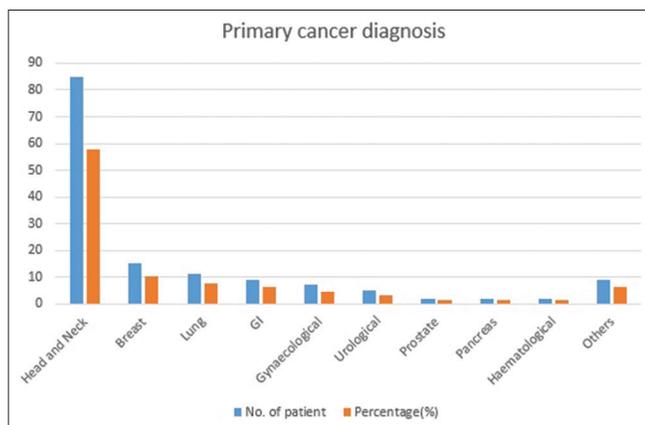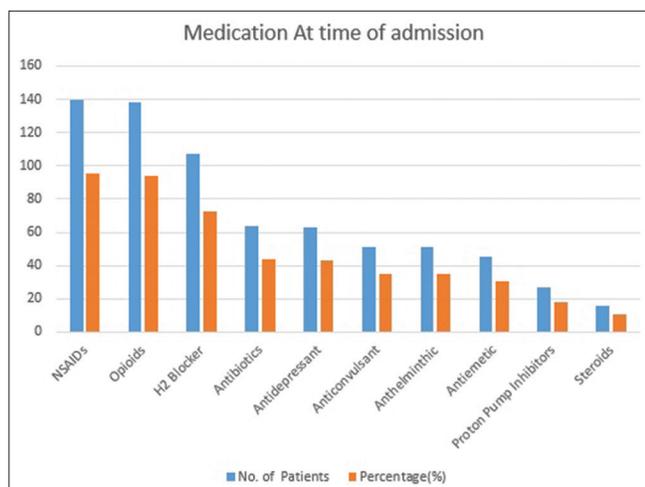

Figure 2: Primary diagnosis.

Figure 3: Patients taking drugs at time of admission.

Table 1: Symptom at time of admission.

Symptoms	Mean (SD)	Number of patients(%) with NRS ≥7
Pain	5.81 (1.61)	58 (39.4)
Fatigue	3.5 (2.41)	28 (19)
Drowsiness	1.98 (2.47)	19 (12.9)
Nausea	2.4 (2.35)	11 (7.4)
Appetite	3.88 (2.52)	28 (19)
Breathlessness	2.26 (2.6)	11 (7.4)
Depression	1.25 (1.91)	3 (2)
Anxiety	3.51 (2.43)	20 (13)
Sleep	4.22 (2.27)	28 (19)
Well-being	4.91 (1.6)	32 (21)

brain metastasis, dehydration, cachexia, dyselectrolytemia, myiasis and h/o substance abuse.

A summary of the delirium characteristics of patients with delirium are summarised in Table 3. Most frequent subtype is mixed and hypoactive followed by hyperactive. Haloperidol was the most commonly used single agent medication to treat delirium followed by combination of haloperidol with midazolam. Other single interventions include hydration, antibiotics and opioids rotation. Counselling of patients and caregivers was performed in all delirium cases. Most of the delirium management included a combination of various treatment strategies including both pharmacological and non-pharmacological measures.

Table 4 summarise outcomes of different types of delirium. In our study, most common type of delirium is hypoactive and mixed subtype followed by hyperactive delirium. Resolution of delirium was higher among hyperactive delirium (78.57%), followed by mixed subtype (50%) and hypoactive (12.5%). Mortality was higher among patient with hypoactive subtype (81.25%), followed by mixed (43.75%) and hyperactive delirium (14.28%).

DISCUSSIONS

The objective of palliative care is to relieve suffering and give the most ideal personal satisfaction for patients and their families. Indications might incorporate agony, depression, shortness of breath, difficulty sleeping and anxiety which are very much related to delirium. Delirium is a profoundly predominant complexity in patients in palliative care settings, particularly towards the end phase of life.[17,18]

Delirium diagnosis was based on diagnostic criterion of DSM-IV and MDAS. Out of 147 patients, 46 (31.29%) had delirium during their admission to hospice centre. Out of them, 27 (18.367%) had delirium at the time of admission. This finding is comparable with study results by Hosie *et al.*[19] 2013 in delirium prevalence at hospice ranging from 13.3% to 42.3%. Palliative intervention encompasses total care to patients and caregivers involving multi-disciplinary team. In our study, mortality was higher among patient who had delirium (47.8%, *n*-46) as compared to those without delirium (9.9%, *n*-101). Mortality was higher with hypoactive subtype (81.25%) as compared to mixed (43.75%) and hyperactive delirium (14.28%). Recovery rate of delirium was higher with hyperactive subtype followed by mixed and hypoactive delirium. Similar results were obtained in study done by Fang *et al.*[20] 2008 with higher mortality rate in patients with delirium and higher risk with hypoactive delirium.

By consensus, haloperidol remains the standard pharmacological drug for symptomatic control.[21,22] Dosing plans are derived from well-qualified assessment and different clinical practice rules as evidence-based information are limited from palliative care. The commonly utilised pharmacologic intervention for delirium in this populace warrant assessment in clinical preliminaries to

Table 2: Admission characteristics of patients admitted to hospice centre.

Covariate	Total, *n* (%)	Delirium, *n* (%)	No Delirium, *n* (%)	*P*-value
All patients	147 (100)	46 (100)	101 (100)	
Age, years				
<50	69 (46.9)	24 (34.7)	45 (65.21)	0.4764
≥50	78 (53)	22 (28.2)	56 (71.79)	
Sex				
Male	90 (61.2)	31 (34.4)	59 (65.55)	0.3627
Female	57 (38.7)	15 (26.3)	42 (73.68)	
ECOG status				
1	39 (26.5)	5 (12.8)	34 (87.17)	<0.0001
2	51 (34.6)	7 (13)	44 (86.27)	
3	42 (28.5)	21 (50)	21 (50)	
4	15 (10.2)	13 (86.6)	2 (13.33)	
PAP score				
A (0–5.5)	94 (63.9)	16 (17)	78 (82.97)	<0.0001
B (5.6–11)	39 (26.5)	19 (48.7)	20 (51.28)	
C (11.1–17.5)	14 (9.5)	11 (78.5)	3 (21.42)	
Comorbid				
HTN	12 (8.1)	4 (33.3)	8 (66.66)	0.9104
DM	7 (4.7)	2 (28)	5 (71.42)	
CAD	2 (1.3)	1 (50)	1 (50)	
Neurological	2 (1.3)	1 (50)	1 (50)	
Thyroid ds	3 (2)	0	3 (100)	
Past 3 month				
Pal.RT	16 (10.8)	5 (31.2)	11 (68.75)	0.3268
Pal.CT	11 (7.4)	3 (27.2)	8 (72.72)	
Pal-RT+Pal-CT	1 (0.02)	1 (100)	0	
H/O of substance abuse				
Tobacco	72 (48.9)	15 (20.8)	57 (79.16)	0.0063
Tobacco+alcohol	11 (7.4)	7 (63.3)	4 (36.36)	
Risk Factors				
Dyselectrolytemia	52 (35.3)	11 (21)	41 (78.84)	<0.0001
Myiasis	51 (34.6)	8 (15.6)	43 (84.31)	
Cachexia	41 (27.8)	19 (46.3)	22 (53.65)	
Dehydration	17 (11.5)	15 (88.2)	2 (11.76)	
Brain metastasis	8 (5.4)	5 (62.5)	3 (37.5)	

ECOG: Eastern cooperative oncology group, HTN: Hypertension, DM: Diabetes mellitus, CAD: Coronary artery disease, CT: Chemotherapy, RT: Radiotherapy

inspect dosing and titration regimens, various routes of administration and safety and efficacy compared with placebo. Delirium management is multidimensional and incorporates the distinguishing proof of aggravating and precipitating factors. Haloperidol remains the standard practice for symptoms management. Further, great collective exploration researching the suitable treatment of this perplexing syndrome is required.

Delirium can often be traced to one or more contributing factors and the main four risk factors statistically significant found in this research are brain metastasis, dehydration, cachexia, dyselectrolytemia and myiasis. Other studies done by Lawlor *et al.* in 2000 and Casarett *et al.* in 2001 have reported similar risk factors of delirium such as brain metastasis, dehydration and metabolic factors (hyponatremia, hypercalcemia, etc.).[23,24] Other risk factors such as age, gender, associated comorbidities; h/o palliative RT and CT in the past 3 months were found statistically insignificant in our study.

Study limitation

In this study, diagnosis of delirium depended just on indicative measure of DSM-IV and MDAS without Psychiatric Consultation. With pandemic less sample was gathered. Extensive intervention was subverted as most of the respondents were advanced cancer patients and with numerous medical issue investigations were limited.

CONCLUSION

- An identification and assessment of delirium are vital for acceptable end of life care within the palliative

Table 3: Summary of clinical characteristics of patients with delirium.

Covariate	Total (%)
Delirium subtype	
Hyperactive	14 (30.4)
Hypoactive	16 (34.7)
Mixed	16 (34.7)
Aetiology of delirium	
Multifactorial	18 (39.1)
Terminal disease	10 (21.7)
Infection	7 (15.2)
Unknown	7 (15.2)
Medication	4 (8.6)
Medication used for treatment of delirium	
Haloperidol	38 (82.6)
Haloperidol+Midazolam	20 (43.4)
Antibiotics	15 (32.6)
Hydration	9 (19.5)
Antibiotics+Hydration	7 (15.2)
Opioids rotation	8 (17.3)
Resolution of Delirium	
Yes	21 (45.6)
No	25 (54.3)
Discharge disposition	
Death	22 (47.8)
Home	24 (52.1)

Table 4: The outcome of different types of delirium.

Delirium Subtype	Outcome	No	Percentage	Total (%)
Hyperactive	Recovered	11	78.57	14 (30.4)
	Death	2	14.28	
Hypoactive	Recovered	2	12.5	16 (34.7)
	Death	13	81.25	
Mixed	Recovered	8	50	16 (34.7)
	Death	7	43.75	

care in light of the fact that the presence of delirium is related with morbidity, mortality, prolonged ICU hospitalisation, expanded time on a ventilator and by and large more prominent medical services costs

- Clinicians should utilise one of a few approved delirium assessment tools to help evaluate and archive cognitive function
- Prevention and recognising the clinical reason for delirium are generally the best method for diminishing the morbidity from delirium
- As the outcomes demonstrate that multicomponent delirium management or projects are generally proficient to lessen the rates of delirium and negative outcomes of delirium
- It was found that palliative care intervention has quite a positive outcome as it not only focus on the mental health of the patients but also of family members who go through the same amount of distress and also help them to communicate properly and manage to settle the mental state and end the life without pain and distress.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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