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"Postoperative Delirium in Patients Operated Under General Anaesthesia in a Multi Speciality Hospital - A Prospective Observational Study"

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Abstract:
Aim: *To study the incidence of Post-operative Delirium in patients operated under general anaesthesia in a multi- speciality hospital using the Confusion Assessment Method for the Intensive Care Unit (CAM- ICU) and to find the subtype of delirium using the Richmond Agitation Sedation Scale (RASS).*
Background*: Delirium is an acute dysfunction of the brain, characterized by changes in the level of consciousness, inattention and disorganized thinking, which can manifest with hyperactive signs (i.e. hyperactive subtype with agitation and restlessness) or hypoactive signs (i.e. hypoactive subtype with lethargy and inattentiveness). Screening for delirium in the Post Anaesthesia Care Unit (PACU) and in the postoperative hospital wards is generally not part of routine clinical practice. Richmond Agitation-Sedation Scale (RASS) is another commonly used screening method which provides a single platform that is intuitive, easy to use, and includes both agitation and sedation related parameters. A lot of information comes from studies in the West, where progressively increased interest has been shown to explore this issue in postoperative patients. The present study has been planned to find the incidence and subtype of delirium in postoperative patients catered by us.*
Materials and Methods*: In this Prospective observational study 300sample population was taken who underwent elective surgery under general anesthesia. Patients were assessed for delirium and its subtype using Confusion Assessment Method for the Intensive Care Unit (CAM- ICU) score and Richmond Agitation-Sedation Scale (RASS) in the post operative period immediately, after 24 hrs &then after 48 hours in the post operative period. All observations were stratified and further evaluated.*
Results*: 56 patients developed Post-operative delirium immediately in the post operative period. After 24 hours, 27 cases had delirium out of which only 6 were of new onset. After 48 hours, 6 cases had delirium, but all were old cases*
Conclusion: *Incidence of delirium was similar with both the assessment tools namely CAM-ICU & RASS scale. Hypoactive delirium with incidence of 77.4% was the most common observed subtype followed by mixed delirium (16.1%).*
Key Word*: Richmond Agitation-Sedation Scale, Post-operative delirium Confusion Assessment Method.*

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I. Introduction

Delirium is an acute dysfunction of the brain, characterized by changes in the level of consciousness, inattention and disorganized thinking, which can manifest with hyperactive signs (i.e. hyperactive subtype with agitation and restlessness) or hypoactive signs (i.e. hypoactive subtype with lethargy and inattentiveness). It is quite common throughout the hospital. Almost 60-80% mechanically ventilated patients and 20–50% of patients with lower severity of illness develop delirium at some point of time during their stay in the hospital.[(1)] Its prevalence is 10-24% in the adult general medicine population and 37-46% in the general surgical population.[(2)]

Delirium has been independently associated with significant distress to both patient and the health care professionals. These include increased length of hospital stay, inpatient mortality, long term mortality, cognitive decline, focused requirement of hospital care, functional impairment, healthcare cost and mental and economic burden to the patient and relatives[(3-5)]. Therefore, delirium is being viewed as a matter of concern.

Postoperative delirium (POD) is a form of delirium, manifesting in patients who have undergone surgical procedures and anesthesia, and usually peaks between one and three days after the operation. Postoperative delirium rates incidence ranges from 9% to 87%, depending on patient age and the type of surgery.[(2)]

Screening for delirium in the Post Anaesthesia Care Unit (PACU) and in the postoperative hospital wards is generally not part of routine clinical practice. Delirium is often overlooked in hospitalized patients unless a routine screening program is implemented as part of protocolized approach. New validated screening tools to identify delirium are being implemented in these settings.[6, 7]

Various screening tools for identifying delirium are in use, with its own set of advantages and disadvantages. A commonly used delirium screening tool is the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). It has been validated, in detecting delirium in mechanically ventilated ICU patients, by two systematic reviews reporting a sensitivity of 76–80% and specificity of 96%.[8, 9] There are limited studies documenting its applicability in the PACU setting, but it appears logical to use this screening tool in PACU and postoperative setting also as most of the patients receiving general anaesthesia need sedation and mechanical ventilation similar to Intensive care unit (ICU). [10]

Richmond Agitation-Sedation Scale (RASS) is both reliable and valid in critically ill adults with and without mechanical ventilation and sedation.[11] This scale has been used frequently in research setting and also in the clinical practice to monitor the patients with delirium.[12]

A lot of information comes from studies in the West, where progressively increased interest has been shown to explore this issue in postoperative patients. Moreover, most of the Indian as well as western studies have focused on elderly population. Therefore, the need to find out the incidence in younger adults is imperative.

The present study has been planned to find the incidence and subtype of delirium in postoperative patients catered by us.

II. Material And Methods

This prospective observational study was conducted in the Department of Anaesthesia and Critical Care, Tata Main Hospital, Jamshedpur which is a 940 bedded multidisciplinary teaching hospital. Total study population taken was 400, out of which 80% was taken as the sample size. Time frame to address the study was from 15 December 2016 to 15 November 2017. Patients undergoing elective surgery under general anaesthesia were included. Patients with aged below 18 years, having neurological, psychiatric, neuromuscular disorders, hearing & visual impairment, with addictions – Alcohol, Psychotropic drugs and with language barrier were excluded from study.

Study was approved by ethical Committee, Tata Main Hospital, Jamshedpur, Jharkhand.

Sample size calculation with justification

Taking α at 0.05 and desired power of study is 80% the sample size needed was 300.

We accepted a $p<0.05$ as significant. We mean that we are ready to accept the probability that the result observed due to chance is 5%. Confidence level = 95%, Confidence interval = 2.02, Population = 400, Sample size = 300

Exclusion criteria = 20

Finding the smallest sample size required to achieve a fixed margin of error, using simple random sampling.

$n = \sigma^2 (Z_\beta - Z_\alpha)^2 / \Delta^2$

Where 'n' was the required sample size. Taking the α at 0.05 and desired power of study is 80%

Therefore, $n = [(31.29)^2 (0.8416 - 1.96)^2] / (2.02)^2 = 300.125 \approx 300$

Hence, this is the required sample size.

III. Methodology

Pre anaesthetic checkup:

A detailed history was elicited including history of any major illness or disease in the past. General physical examination and systemic examination of each patient was performed. Appropriate biochemical, hematological, and radiological investigations was done as per hospital protocol. Patients were explained about the study and informed consent was taken.

Anaesthesia Technique:

Fasting status was confirmed before the patients were taken to the operation theatre. After shifting the patients to the operative room, standard monitors were attached which included ECG, Pulse oximeter and NIBP and the baseline parameters were recorded. The patients IV access were secured with 18G venous cannula under aseptic precautions and 0.9% Normal Saline infusion (6ml/kg) was started.

Patients were preoxygenated with 100 % oxygen for 3 minutes. Midazolam 1 mg IV was given before induction. Anesthesia was induced with Fentanyl 2 µgm/kg IV or Morphine 0.1mg / kg IV or Pethidine 1mg/kg IV and it was followed by Propofol 2.5 mg/kg IV slowly over 30 seconds. After confirming loss of response to verbal commands, Succinylcholine 1.5 mg/kg IV was given to facilitate intubation. Laryngoscopy was done

with macintosh blade size 3 or 4 after disappearance of fasciculations. All laryngoscopies were performed by experienced anaesthesiologist. Anesthesia was maintained with Isoflurane 0.5-1% in 30:70 mixture of oxygen and nitrous oxide. Bolus intravenous dose of Vecuronium at 0.08 mg/kg followed by intermittent dose of 0.02 mg/kg was used for muscle relaxation. The patients were ventilated maintaining an end tidal CO_2 levels between 30 & 35 mm Hg. During the operation, Heart Rate, Blood pressure and SpO_2 levels were recorded every 5 mins. After the completion of surgical procedure, patients were reversed with Neostigmine 0.05mg/kg IV and Glycopyrrolate 0.08mg/kg IV and extubated followed by shifted to recovery room for postoperative monitoring.

IV. Observation

In the post operative period, timing of initiation of delirium assessment was standardized. Patients were assessed for Aldrete score and a score > 9 indicated an appropriate level of wakefulness, hemodynamic and respiratory stability for discharge.[13] Delirium was assessed once these criteria were fulfilled. Patients were assessed for delirium and its subtype using Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) score and Richmond Agitation-Sedation Scale (RASS) in the post operative period immediately, after 24 hrs & then after 48 hours in the post operative period. Hyperactive delirium was defined as present in subjects with all positive daily RASS scores (ranging from +1 to +4) associated with every positive CAM-ICU assessment. Hypoactive delirium was defined as present in subjects with all neutral or negative daily RASS scores (ranging from 0 to −3) associated with every CAM-ICU positive assessment. Mixed type delirium was defined as present when daily RASS scores included both positive values (ranging from +1 to +4) or negative values(ranging from 0 to −3) associated with every positive CAM-ICU assessment. Symptomatic patients were followed up by Psychiatrist and necessary treatment was provided.

Statistical Methods

Statistical testing was conducted with the statistical package for the social science system version SPSS 17.0.

Continuous variables are presented as mean ± standard deviation, and categorical variables are presented as absolute numbers and percentage. The comparison of normally distributed continuous variables between the groups was performed using Student's t test. Nominal categorical data between the groups were compared using Chi-square test. A p value <0.05 was considered statistically significant.

V. Observation And Result

1. Demographic parameters :

Table1; shows the demographic parameters. In our study males were 44.3% and females were 55.7%. The mean age was comparable between the two groups.

Table 1

Distribution	Number of patients	Mean Age
Male	133 (44.3%)	50.68
Female	167 (55.7%)	49.71
Total	300	50.14

2. CAM-ICU & RASS Scale

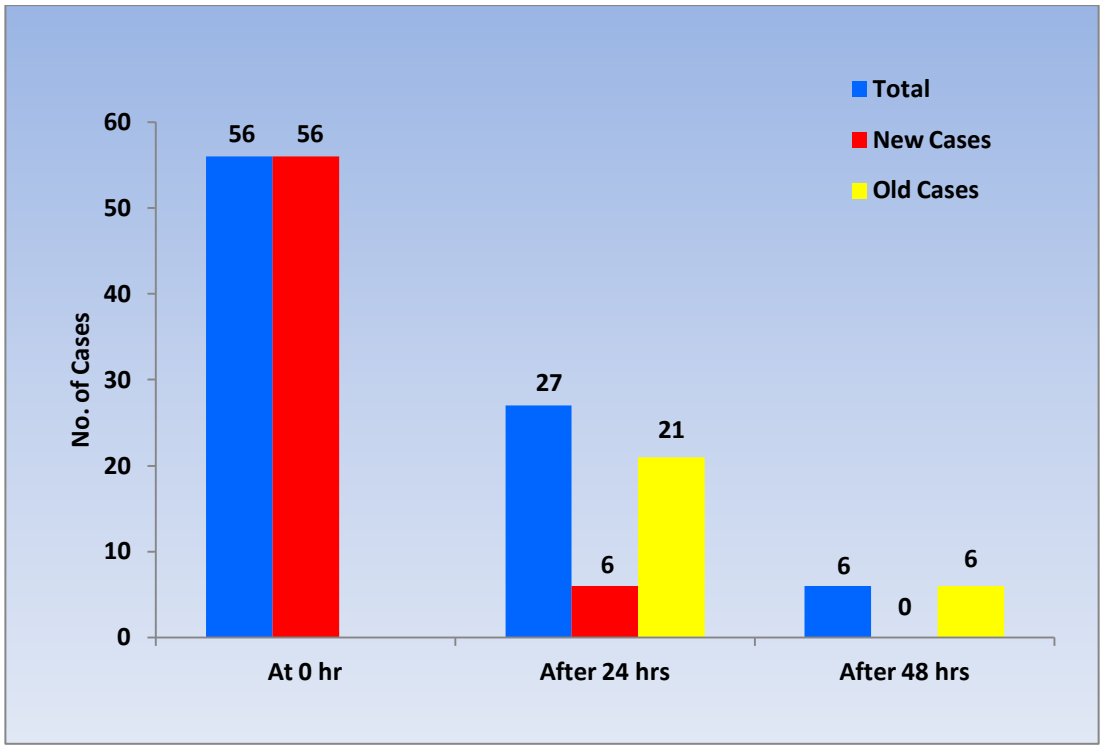
Table 2 shows number of delirium cases detected by the CAM-ICU and RASS scale. Both were found to be similar.

Table 2

Assessment Tool	Total patients	Delirium Present	Delirium Present %
CAM-ICU	300	62	20.7%
RASS	300	62	20.7%

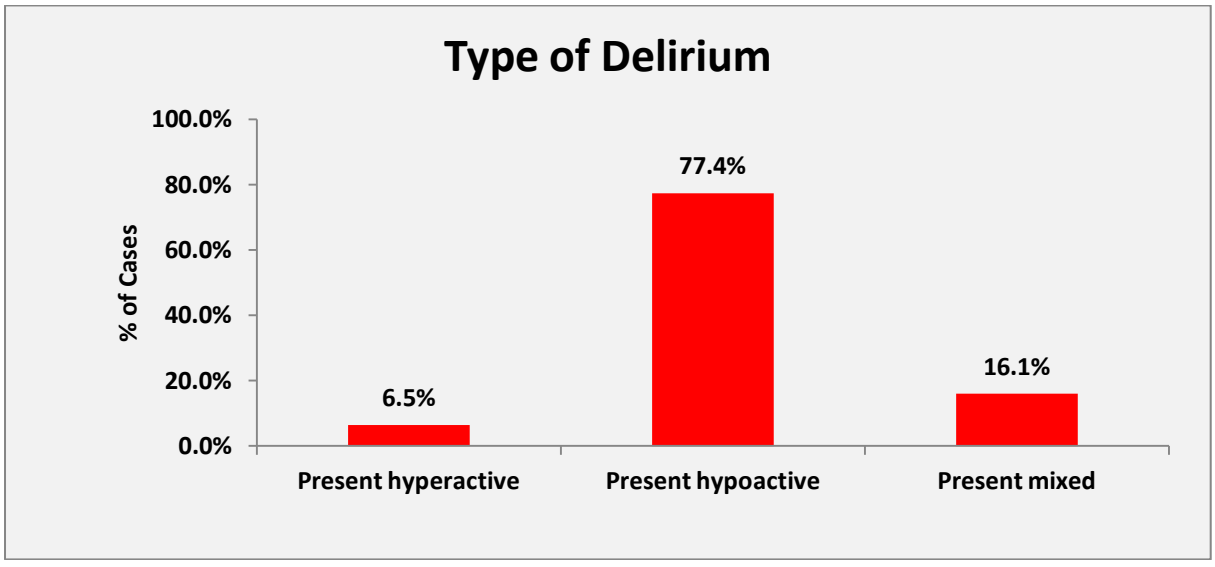
3. Development of delirium (Time period)

Graph1 shows that at 0 hour, Delirium was observed in 56 cases. After 24 hours, 27 cases had delirium out of which 6 were of new onset. After 48 hours, 6 cases had delirium but none were of new onset.

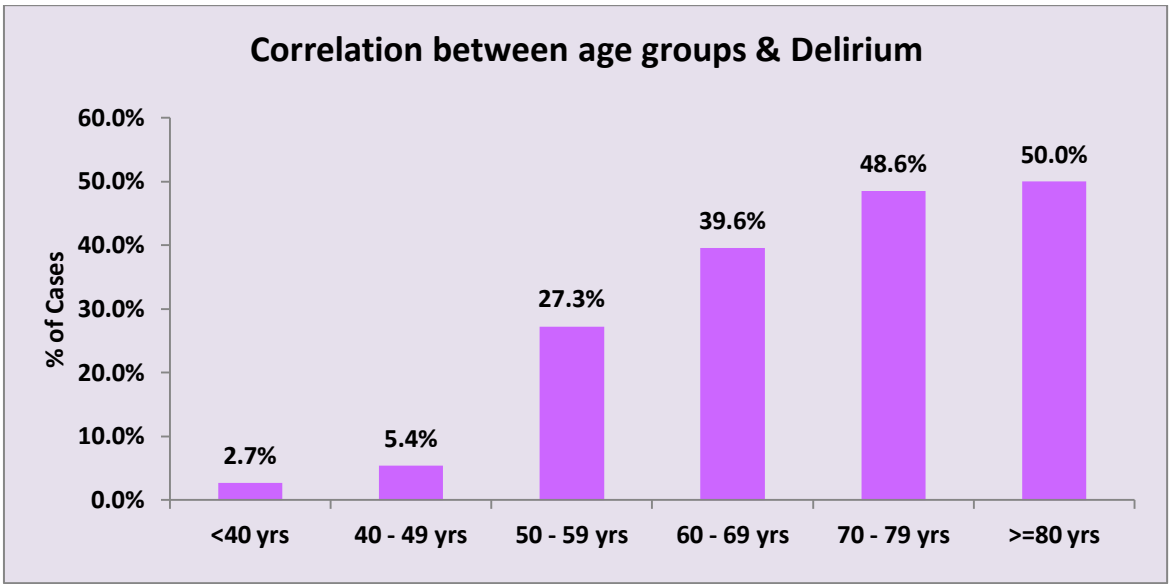


4. Type of delirium

Graph 2 Represents the subtype of delirium detected by the RASS scale. Hypoactive delirium was most common with an incidence of 77.4%, followed by mixed subtype which was 16.1% and least common was hyperactive delirium, with incidence of 6.5%.

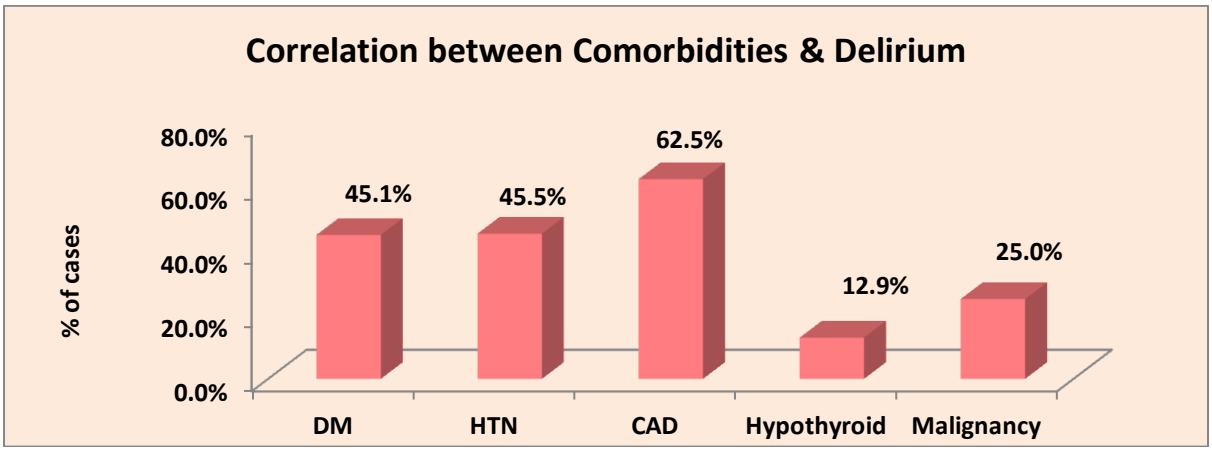


Graph 3 represents the age wise distribution of Delirium present patients. Incidence of Delirium was higher with increasing age. Chi- Square test showed p value < 0.001, which was statistically significant.



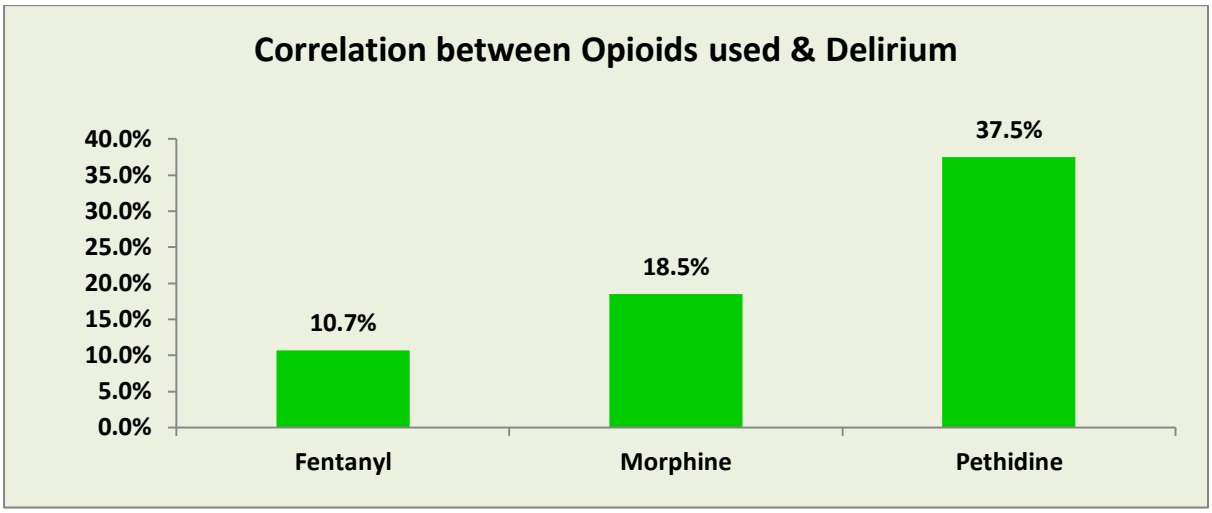
5. Co-relation of Delirium with type of Co-morbidities

Graph 4 represents different co morbidities among patients and development of delirium. Chi square test showed p value < 0.001, which was statistically significant for DM, HTN and CAD and these correlated with development of Delirium. The result was statistically not significant for patients with Hypothyroidism and Malignancy.



6. Co-relation of Delirium with use of Opioid type

Graph 5 represents the correlation between the opioid type used and development of delirium. Delirium was found to be maximum with use of Pethidine. Chi square test showed p value < 0.001, which was statistically significant.



7. **Co-relation of Delirium with use Midazolam**

Table 3 represents relation of Delirium with use of Midazolam. Chi square test showed p value of 0.523, which was not statistically significant.

Midazolam used	Total Cases	Delirium Present		P Value
		Frequency	%	
Yes	156	30	19.2%	0.523
No	144	32	22.2%	
Total	300	62	20.7%	

VI. Summary Of Observation

Incidence of Post-operative delirium was similar using the two scales namely CAM-ICU and RASS scale. 56 patients developed Post-operative delirium immediately in the post operative period. After 24 hours, 27 cases had delirium out of which only 6 were of new onset. After 48 hours, 6 cases had delirium, but all were old cases.

Hypoactive delirium was found to be the most common with an incidence of 77.4%.This was followed by Mixed subtype which was 16.1% and least common was Hyperactive delirium with an incidence of 6.5%. Development of Post-operative delirium was significantly higher in patients suffering from DM, HTN and CAD, but did not co-relate well with patients suffering from Hypothyroidism & malignancy. Correlation of development of Post-operative delirium with the use of Opioid type showed that use of Pethidine was significantly associated with the development of delirium, as compared to the use of Morphine & Fentanyl. Development of Post-operative delirium did not show any correlation with use of Midazolam.

VII. Discussion

A total of 300 patients undergoing elective surgery requiring administration of general anaesthesia were included in the study. Patients were assessed for delirium and its subtype using CAM- ICU score and RASS in the immediate post operative period, after 24 hours and after 48 hours. Our results were similar to the findings of the previous studies done by Gleason et al[14] (24%) and Chrispal et al[15] (21%). However, it was much less than the incidence reported by the studies done by Oh et al[16] (34%), Neufeld et al[13] (45%) and Moskowitz et al (44%). Barring the studies done by Gleason et al[14] where 566 patients were enrolled and 431 patients included in the study conducted by Oh et al[16], the other reports had lesser study population ranging from 81 to 172 patients.[15] The lower incidence of delirium in our study was similar to another study published from Southern India. They found 21% delirium in 81 patients.

In the present study two assessment tools, CAM-ICU and RASS were used in conjunction to find out the incidence of delirium and its subtypes. Same assessment tools were used by Robinson et al to find the motor subtypes of delirium. E card et al[1] also used similar tools but they concentrated on the incidence of emergence delirium. Similarly, CAM-ICU also has the advantage of being easy and more practical in the post operative period but it fails to identify the subtypes of delirium unlike RASS score.[12] Hypoactive delirium was observed as the most common form of delirium with an incidence of 77.4%, followed by Mixed (16.1%) and Hyperactive

form (6.5%) in our study. Robinson et al, Pandharipande P et al, Marcantonio E et al[16] had done similar stratifications and they too reported higher incidence of hypoactive delirium which was 68%, 64% and 71% respectively.

Predisposing risk factors for developing delirium include functional impairment, preexisting neuropsychiatric conditions, and the presence of multiple medical co morbidities like heart failure, renal dysfunction, diabetes mellitus, and vascular disease. Parente D et al concluded that congestive heart disease was an independent risk factor for POD. In the present study, higher incidence was noted in patients having preexisting hypertension, diabetes mellitus and coronary artery disease. (p value < 0.001).

Review of literature showed that pethidine accounted for approximately 30% of all cases of delirium and played a major role in postoperative delirium. Normeperidine, a metabolite of Pethidine, has been considered to be a potent neurotoxic agent with significant anticholinergic activity. The combination of direct neurotoxic effect and strong anticholinergic activity might have been responsible for delirium in patients treated with pethidine.. Marcantonio ER et al[16] concluded in his study that delirium was significantly associated with exposure to pethidine and benzodiazepine. We had a similar experience and observed 37.5% incidence of delirium with pethidine group as compared to 10.7% in fentanyl treated patients and 18.5% in patients managed with morphine. This was found to be statistically significant (p value < 0.001). In benzodiazepines group, the incidence was only 19.2% and it was not statistically significant (p value= 0.523). E. Card et al[1] also failed to find a significant association of delirium with benzodiazepine exposure.

VIII. Conclusion

Postoperative delirium is a complication that is linked to multiple predisposing and precipitating factors and needs attention so that it can be managed promptly and effectively.The incidence of Post-operative delirium as per our observational study was 20.7%. Most of the patients had delirium at the time of admission to PACU, while few developed the same in the next 24 hrs.The incidence was similar to another Indian study, but was less as compared to the Western reports.

Incidence of delirium was similar with both the assessment tools namely CAM-ICU & RASS scale. Hypoactive delirium with incidence of 77.4% was the most common observed subtype followed by mixed delirium (16.1%), in our study. It was also noted that increasing age, presence of co-morbidities, type of surgery contributed significantly to the development of Post-operative delirium in the present series. Delirium was more common with the use of Pethidine (Opioids).

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