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## Prospective study of incidence and risk factors of post-operative delirium following hip/femur surgery in elder patients (age > 60years) in tertiary care hospital

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### Abstract

**Introduction:** Hip fracture represents around 1/4 of the geriatric fractures. Over 90% of hip and femur fracture patients are older than 65 years and have pre-existing medical co-morbidities. Postoperative Delirium (POD) is one of the common complications in elders (incidence 5.1%-52.5%) affecting quality of life and may prolong hospital stay. Oh YK *et al* investigated incidence and risk factors for POD in geriatric patients and assessed delirium using Confusion Assessment Method and Mini Mental State examination.

**Methods:** This was a prospective study design; to evaluate preoperative and intra-operative risk factors for delirium in 145 elder patients (age > 60yrs) following elective hip/femur surgery in tertiary care hospital, primarily focusing on incidence of POD and investigated independent association of risk factors with POD. Confusion Assessment Method was used for assessing POD.

**Results:** The incidence of POD due to preoperative, intra-operative and postoperative risk factors was 26, 25.28 and 48.5 respectively.

**Conclusion:** The incidence of delirium increases post operatively, the incidence being 40 in our study. Age > 70years, abnormal serum sodium and potassium and diabetes mellitus were found as preoperative risk factors; general anesthesia and increased duration of surgery for intra-operative risk factors; VAS score >6 and analgesic usage for postoperative risk factors for development of POD. We suggest that Confusion Assessment Method can be used for assessing POD in elder patients pre and postoperatively.

**Keywords:** Elder patient, hip/femur surgery, postoperative delirium, risk factors

### Introduction

There is global rise in elder population (Silver Tsunami) <sup>[1]</sup>. With rising surgical illnesses in elderly. Delirium is one of the common post-operative complications in elder trauma patients, may increase morbidity/ mortality, prolonged hospital stay and cost of treatment <sup>[2]</sup>. The incidence of postoperative delirium (POD) ranges from 5.1%-52.5% <sup>[3]</sup>. Hip fracture represents around 1/4 of the geriatric fractures <sup>[4]</sup>. Over 90% of hip and femur fracture patients are older than 65 years and have pre-existing medical co-morbidities <sup>[5]</sup>. Acute Ortho-geriatric units combined with medical management results in successful outcome <sup>[6-8]</sup>. Delirium is an acute confusional state characterized by fluctuating symptoms such as inattention, disturbance of consciousness or disorganized thinking. Other symptoms include disorientation, memory impairment, perceptual disturbances, altered psychomotor activity and disturbed sleep wake cycle <sup>[9]</sup>. Cognitive complications appear in approximately 10% of patients after hip fracture surgery in elders (> 65 years); use of acrylic cement for prosthetic implantation induced inflammatory response remains important cause <sup>[10]</sup>.

To evaluate delirium easily and quickly, many assessment tools have been developed e.g. Confusion Assessment Method (CAM), Mini Mental State Examination (MMSE), Delirium Writing Test, The Diagnostic and Statistical Manual of mental disorders <sup>[3, 11, 12]</sup>. Oh YK *et al* <sup>[3]</sup> investigated incidence and risk factors in acute POD in geriatric patients and assessed delirium using CAM and MMSE. The incidence of POD is dependent on preoperative and intra-operative risk factors and predisposing risk factors which accumulate with ageing.

Hence present study was done to evaluate preoperative and intra-operative risk factors for POD in elder patients (age>60 years) after hip and femur surgery primarily focusing on incidence of POD and investigated independent association of risk factors with POD.

### Methods

This was tertiary care hospital based prospective study, conducted with 145 elder patients (age>60 years) undergoing elective hip/ femur fracture surgery.

**Research question:** Does the incidence of POD increase in patients >60 years of age undergoing hip/ femur surgery. We hypothesized that, there is increase in incidence of POD in patients > 60 years of age after hip/femur surgery.

**Study design:** Prospective, observational study.

**Study Duration:** December 2019 to September 2021.

**Study area:** at tertiary care centre in department of Anesthesiology.

**Study population:** All patients of age > 60 years fulfilling inclusion criteria.

**Sample size:** By considering the proportion of occurrence of delirium is 54% [13]; sample size was calculated by using the following formula;

$$n = \frac{Z^2 pq}{d^2}$$

Where, n= sample size, Z = Standard normal variate for  $\alpha = 0.05$  (95% CI) = 1.96, p= proportion (%) under interest; q= 100-p, d= allowable error 15% of P = 8.1%

By substituting the values in formula, sample size of 145 patients were selected for the study.

### Inclusion criteria

Patients age > 60 years, ASA grade I/II/III, male/female gender, elective hip surgery (Total hip replacement, hemiarthroplasty, acetabular plating) or femur surgery (Femur nailing, CC screw fixation, femur plating).

### Exclusion criteria

Preoperative delirium or preoperative cognitive dysfunction, neuropsychiatric illness, emergency surgery, drug abuse.

### Technique

After approval from Institutional Ethics Committee and Institutional Review Board, informed consent was taken from total 145 patients satisfying inclusion criteria. A thorough pre-anesthetic evaluation of all patients was done which also included details of education, marital status, H/o alcohol consumption, smoking, major medical/surgical illness, Body mass index, medications history. Systemic examination was done thoroughly with neurological examination. Preoperative assessment of delirium was done using CAM method. All patients were fasted for 6 hours preoperatively. In operation theatre, intravenous line was set up using 20G canula on upper limb and started intravenous Ringer's Lactate at 15ml/kg. The multipara monitor (ECG,

NIBP and SpO<sub>2</sub>) was connected to the patient. Monitoring of systolic blood pressure-SBP, diastolic blood pressure-DBP, heart rate-HR, Electrocardiogram and oxygen saturation-SPO<sub>2</sub> were recorded prior to induction of anesthesia and intraoperatively. **Premedication:** to all patients: Inj. Ondansetron 0.08mg/kg intravenous was given 30 minutes before induction of anesthesia. Patients were given either general anesthesia or regional anesthesia (spinal and/or epidural) by following method. General anesthesia by standard balanced anesthesia technique using preoxygenation, premedication Glycopyrrolate 0.2 mcg/kg, midazolam 0.03mg/kg and fentanyl 1mcg/kg intravenous, induction with Thiopentone 3-5 mg/kg and succinylcholine 2 mg/kg intravenous followed by intubation. Anesthesia was maintained with O<sub>2</sub>, N<sub>2</sub>O, isoflurane and vecuronium as muscle relaxant. After completion of surgery patients were reversed with intravenous Glycopyrrolate 10 mcg/kg and Neostigmine 50mcg/kg and extubated. **Spinal Anesthesia:** Under all aseptic precautions, spinal anesthesia was given using 25G Quincke's spinal needle at L3-L4 or L4-L5 space using 0.5% hyperbaric bupivacaine 3cc. Sensory level was assessed using pinprick method and was achieved at T10 dermatomal level. **Epidural Anesthesia-** In anticipated cases of longer duration surgeries, 18G epidural catheter was inserted before giving spinal anesthesia under all aseptic precautions at L2-L3 or L3-L4 level using 18G Touhey's needle. Epidural anesthesia was maintained using Inj. Lignocaine and Inj. Bupivacaine.

### Recordings

Type of surgery- (Hip surgery or Femur surgery), Type of anesthesia, duration of surgery (minutes), Total intraoperative blood loss (ml), Adverse events—nausea, vomiting, dizziness, dryness of mouth, postoperative VAS Score, postoperative analgesia usage.

### Recordings of Delirium

Assessment of delirium of all patients was noted by the same primary investigator at following time intervals. 1. baseline (preoperatively) 2. Postoperatively after 24 hours of surgery 3. Postop 3rd day 4. Postop 5th day. Confusion Assessment Method (CAM) [14] was used for delirium assessment. It is scored as present or absent by following method. CAM consists of four diagnostic criteria: 1) Acute onset and fluctuating course of cognitive and behavioral impairment, 2) Inattention, 3) Disorganized thinking, 4) Altered level of consciousness. Score delirium as present if meets the following criteria:

(i) Acute Onset or Fluctuating course and (ii) Inattention and Either (iii) Disorganized thinking or (iv) Altered level of consciousness

Patients developing POD were given Injection haloperidol 2.5 mg intravenously 6hourly if required and neuropsychiatric evaluation was done.

### Definitions

Duration of surgery (in minutes) - defined as time interval from skin incision to skin closure in minutes. Intraoperative blood loss (ml) - Blood loss more than maximum tolerable blood loss for that patient was considered as significant blood loss. Abnormal level of serum sodium - <130 or > 150 mmol/L, Abnormal serum potassium level < 3.0 or > 6.0 mmol/L, deranged blood glucose level— fasting < 60 or postprandial 2 hr> 300mg/dl. Postoperatively VAS Score—

Score >6 with Visual Analog Scale, considered as significant score.

### Statistical Analysis

Quantitative data (Age, height, weight, BMI, duration of surgery) was presented as Mean and Standard deviation. Comparison of mean HR, SBP, DBP, MAP, SPO2 was done using ANOVA test. P value < 0.05 was taken as significant. Qualitative data (Gender, ASA grade, adverse events) presented as frequency and percentage. Association among the study group was assessed by Chi-Square test. 'P' value < 0.05 taken as significant. Appropriate statistical software, including but not restricted to MS Excel, SPSS ver. 20 was used for statistical analysis.

### Discussion

Hip and femur fractures endanger the physical and mental health of elder people and quality of life. Delirium is one of the most common complications after hip/femur surgery [15]. There are many hypotheses for POD e.g. central neurotransmitter theory, brain metabolic level change theory, surgical stress theory and neuroinflammation hypothesis [16]. Delirium is an acute brain dysfunction that manifests as distracted attention, declined recognition, disturbances of circadian clock, emotional and mental disorders [17]. Delirium most probably results from an imbalance in synthesis, release and inactivation of neurotransmitters (glutamatergic, dopaminergic and cholinergic pathways) [18], increased level of dopamine and reduced level of acetylcholine [19]. The inflammatory markers lead to prothrombotic state causing reduced cerebral blood flow triggering delirium, increased dopamine and decreased acetylcholine levels [20].

A tertiary care hospital based prospective observational study was conducted with 145 elder (age>60 years) patients to evaluate the incidence of delirium and preoperative and intra-operative risk factors that may contribute to the occurrence of delirium in elder patients undergoing elective hip/femur surgery.

### Demographic variables (Table 1)

In present study, male were more in number as compared to female patients. Mean age of study population was 64.77 years and mean BMI was 22.52 kg/m<sup>2</sup>. This is similar to studies of Oh YK *et al* [3], Wang CG *et al*. [21] and de Jong L *et al* [15].

Oh YK *et al* [3] in their retrospective study investigating the incidence and risk factors of POD in patients older than 70 years who had undergone a neurosurgical operation found mean age of patients was 70.5±4.26 years and 55.5% were male (n=123). de Jong L *et al* [15] studied risk factors for delirium after hip surgery; found mean age of patients 81±8 years, 67% (n=310) were female, and mean age in delirium group was significantly higher (84 vs 80 years). Wang C *et al*. [21] reported incidence increasing with age, rising to 14% in people > 85 years of age.

Mean duration of surgery in our study was 120.13 min; elders with ASA grade 1(45%) were more than ASA grade 2 and ASA grade3. (Table1) de Jong L *et al*. [15] in study assessing the potential risk factors for developing delirium after hip fracture surgery showed 50% (n=225) of patients had ASA score of ≥3.

### Hemodynamic Variables (Table 2)

There was no significant change from preoperative to postoperative mean HR, SBP, DBP, MAP, SPO2 as per ANOVA test ( $p>0.05$ ).

**Adverse Events:** Most common adverse events observed in our study were nausea (25.5%), dryness of mouth 10.3%, vomiting 8.3% and dizziness 5.5%.

### Risk factors for development of post-operative delirium (POD)

#### Preoperative Risk Factors for POD (Table 3)

In present study, pre-operative risk factor of elder patients >70 years for development of POD was seen in 36 cases and had significant association as per Chi-Square test ( $p<0.05$ ). In the age group 60-70 years, 22 patients developed POD but were not statistically significant. Diabetic patients (12 cases) showed significant association with development of POD as per Chi-Square test ( $p<0.05$ ). Abnormal serum sodium (31 cases) and abnormal serum potassium (25 cases) were also preoperative risk factors having significant association with development of POD as per Chi-Square test ( $p<0.05$ ).

Incidence of POD due to pre-operative risk factors was 26 in our study. de Jong L *et al* [15] found age as significant predictor for delirium, with median age of 84 years in delirium group and 80 years in non-delirium group. Xu W *et al*. [22] study of risk factors of delirium after hip fracture surgery revealed preoperative albumin, history of delirium, TSH and age were the independent risk factors for development of POD. Kalisvaart KJ *et al* [23] found that age was an independent predictive factor for delirium in elderly hip-surgery patients.

#### Intraoperative Risk Factors for POD (Table 4)

Intra operative risk factor of general anesthesia had significant association with development of POD as per Chi-Square test ( $p<0.05$ ). Total 37 patients were operated under general anesthesia amongst which 24 patients developed POD. Under regional anesthesia 108 patients were operated amongst which 32 patients developed POD. Duration of surgery >2hours (30 cases) was also an intra operative risk factor having significant association with development of POD as per Chi-Square test ( $p<0.05$ ). There were 74 patients who underwent hip surgery and 71 patients femur surgery in which 30 patients and 26 patients developed POD respectively. There was significant amount of blood loss in 90 patients amongst which 20 patients developed POD. Thus Hip/Femur surgery and intra-operative significant blood loss were not significant risk factors for development of POD.

Incidence of POD due to intra-operative risk factors was 25.28 in our study. Oh YK *et al* [3] retrospective study showed occurrence of POD correlated with factors such as operation performed under local or regional anesthesia, longer operation time (>3.2 hr), severe pain score (VAS>6), postoperative use of narcotic analgesics and prolonged recovery room stay (>90 min). Lee HB *et al* [13] prospective cohort study compared pre- and intra-operative predisposing factors for incident delirium, with and without pre-operative dementia. They observed in the No Dementia group that age, male gender, number of medical comorbidities, pre-operative MMSE score, and an ASA rating



of 4 or above were associated with incident delirium; medical co-morbidities were not associated with incident delirium in either group.

**Duration of Surgery**

The duration of surgery was 90 minutes, 2 hours, 3 hours and 4 hours in 25 patients, 82 patients, 26 patients and 12 patients respectively. In group with duration of surgery of 90 minutes, 6 patients developed POD out of 25 patients. In group with surgery duration of 2 hours, 22 patients developed POD out of 82 patients. In group with surgery duration of 3 hours, 20 patients developed POD out of 26 patients. In the duration of surgery of 4 hours, 10 patients developed POD out of 12 patients. This shows significant association of POD with increase in duration of surgery as per Chi-Square test ( $p < 0.05$ ). Lee HB *et al.* [13] prospective cohort study showed longer duration surgery was significantly associated with higher incidence of delirium in the No Dementia group. More specifically, those with hip fracture repair lasting >2hrs had significantly higher incidence of delirium than those without (31.8% versus 19%). Among the surgery types, intramedullary hip screw procedure was substantially shorter in duration than other procedures and was associated with lower incidence of delirium.

**Postoperative Risk Factors for POD**

In our study, postoperative risk factor of VAS score >6 had significant association with development of POD (53 cases). Analgesic usage (44 cases) were also post-operative risk factors having significant association with development of POD as per Chi-Square test ( $p < 0.05$ ).

Incidence of POD due to postoperative risk factors was 48.5 in our study. This is concordant to studies of, Oh YK *et al.* [3], de Jong L *et al.* [15] and Xu W *et al.* [22]. Oh YK *et al.* [3] retrospective study revealed on multivariate analyses using backward regression method previous dementia or delirium, pre-existent diabetes, the type of operation performed under local anesthesia, and severe postoperative pain requiring opioid analgesics were independent risk factors of POD. Xu W *et al.* [22] studied risk factors of delirium after hip surgery, indicated that resting VAS on

first postoperative day is an independent risk factor for delirium.

**Incidence of POD at different time intervals in postoperative period** (Table 5): On 1<sup>st</sup> post-op day, 40 patients developed POD. On 3<sup>rd</sup> post-op day, 12 patients developed POD. And on 5<sup>th</sup> postop day, 6 patients developed POD. Thus total 58 patients developed POD out of 145 patients. The incidence of POD was 40 in our study.

Oh YK *et al.* [3] retrospective study investigating incidence and risk factors of POD among 224 patients, 48 showed evidence of POD by postoperative day 3. POD appeared on postoperative day 1 in 35 patients, on postoperative day 2 in 11 patients, and on postoperative day 3 in 2 patients. Similar observations were noted in prospective cohort studies of Lee HB *et al.* [13], showed longer duration of surgery was significantly associated with higher incidence of delirium in the No Dementia group.

**Limitations and future scope of study**

As patients were followed up postoperatively for 5 days, we could not determine delayed onset POD after discharge. This study did not included patients below 60 years of age, other specialties surgeries & no comparison group. Follow up of patients for POD over long duration postoperatively and in surgeries of prolonged duration can be studied.

**Application:** Assessment of delirium by using CAM can be implemented routinely in preoperative evaluation and postoperatively in elderly.

**Table 1:** Demographic data

Parameters	Range	Mean ± SD
Age (years)	60-70	64.34 ± 3.34
	70-82	78.54 ± 2.35
	60-82	64.77 ± 3.29
Height (cm)	141-172	152.48 ± 6.25
Weight (kg)	44-89	52.36 ± 6.75
BMI (kg/m <sup>2</sup> )	18.5-30	22.52 ± 3.46
Male/ Female (n, %)	94/ 51	64.8% / 35.2%
ASA Grade I/II/III (n, %)	65/55/25	45% / 38% / 17%
Duration of surgery (min)	145	120.13 ± 4.24

**Table 2:** Comparison of mean HR, SBP, DBP, MAP, SPO2.

Variable	HR (beats/min)	SBP mmHg	DBP mmHg	MAP mmHg	SPO2 %
	Mean + SD	Mean +SD	Mean + SD	Mean + SD	Mean +SD
Preoperative	86.13± 8.27	114.93±13.57	79.13± 8.81	91.06±11.19	99.64± 0.49
At Induction	88.14 ± 9.20	115.82± 9.59	85.42± 4.64	97.69± 5.81	99.67± 0.49
Intra operative	85.81 ± 3.91	117.84± 3.24	80.05± 3.65	90.31± 4.48	99.47± 0.51
Postoperative	76.42 ± 2.03	120.54± 4.67	88.33± 3.42	93.53± 3.17	98.83± 0.38

**Table 3:** Preoperative risk factors for development of POD

Pre-operative risk factor	POD Absent (n)	POD Present (n)	p value
60-70 years	69	22	>0.05
>70 years	18	36	<0.05
Male	58	36	>0.05
Female	29	22	>0.05
Alcohol abuse (+)	42	11	>0.05
Lab investigations			
Abnormal Serum Sodium	56	31	<0.05
Abnormal Serum Potassium	15	25	
Abnormal Serum Glucose	28	12	

Preexisting co morbidities	61	40	>0.05
Diabetes	21	12	<0.05
Hypertension	20	10	>0.05
Others (BA, IHD, CVA, Seizures)	20	18	>0.05
<b>Lab investigations</b>			
Hb gm%	12.11	12.6	>0.05
Blood urea mg/dl	18.13	20.1	
Serum creatinine mmol/l	82.11	91.4	
Total protein gm/dl	6.11	5.13	
Albumin gm/dl	3.91	4.52	
Globulin gm/dl	25.17	30.11	

**Table 4:** Intra operative risk factors for development of POD

Intra operative risk factor	POD Absent	POD Present	P value
General/ Regional anesthesia (Number of patients)	13/76	24/32	<0.05
Duration of surgery (>2hrs)	8	30	<0.05
Hip/Femur surgery	44/45	30/26	>0.05
Intra-operative blood loss (significant/ Not significant)	70/40	20/15	>0.05

**Table 5:** Distribution of POD in the postoperative period

Variable	Post-op Day 1	Post-op Day 3	Post-op Day 5
POD Present	40	12	6
POD Absent	105	93	87

**Conclusion**

The incidence of delirium increased post operatively, the incidence being 40 in our study.

The incidence of POD due to preoperative risk factors was 26 and due to intra-operative risk factors was 25.28. The incidence of POD due to postoperative risk factors was observed 48.5 as secondary outcome.

Also we found that, age > 70years, abnormal serum sodium and potassium and diabetes mellitus as common preoperative risk factors; general anesthesia and increased duration of surgery as intraoperative risk factors; VAS score >6 and analgesic usage as postoperative risk factors for development of POD.

**Conflict of Interest:** Not available

**Financial Support:** Not available

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