Identification of factors contributing to the development of postoperative delirium in geriatric patients with hip fractures- A prospective study

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ABSTRACT

Introduction: Geriatric hip fractures are a major cause of concern globally and often a frequent reason for morbidity and mortality. Postoperative delirium (POD) is a frequent but often under-diagnosed complication, especially after a major hip surgery. Some of the factors that have been associated with POD are diabetes, high American Society of Anesthesiologists (ASA) grading, electrolyte imbalance, and blood pressure fluctuations. Malnutrition as a risk factor is only recently being recognized. Although there are many possible risk factors reported, they are quite conflicting and not very clear. Therefore, we have attempted to conduct this study to identify the potential risk factors for the development of POD in patients with hip fractures. Materials and Methods: A prospective observational study was performed on 110 geriatric hip fracture patients admitted to tertiary health care in South India. Data regarding preoperative blood investigations, ASA grading, hypertension and diabetes status, MNA (mini nutritional assessments) status, serum albumin, and serum electrolytes values were recorded. The Confusion Assessment Method tool (CAM) was used to diagnose delirium in the postoperative period. Statistical analysis was done for various factors influencing the occurrence of POD. Results: Among the total of 110 cases of geriatric hip fractures patients, 44.5% of the patients developed postoperative delirium. Advancing age, hypoalbuminemia, malnourishment, and uncontrolled diabetes played an important role to the development of post operative delirium in patients with hip fractures. Conclusion: Advancing age, hypoalbuminemia, malnourishment, and uncontrolled diabetes are strong predictors for the development of postoperative delirium in geriatric hip fracture patients. Since age is a non-modifiable risk factor, interventional strategies aimed at correcting modifiable risk factors like nutrition, serum albumin levels, and diabetes control play an important part in preventing delirium in the postoperative period in elderly hip fracture patients. MeSH terms: Hip Fractures, Postoperative Complication, Delirium, Nutrition Assessment, Serum Albumin

Keywords: Delirium, diabetes, elderly, hip fracture, hypoalbuminemia, nutrition

Introduction

Geriatric hip fractures are a major cause of concern globally and often a frequent reason for morbidity and mortality. The incidence is expected to rise fourfold to 6.26 million by 2050.[1] Early surgical intervention and postoperative rehabilitation have become the treatment of choice for patients...
with hip fractures. Postoperative delirium (POD) is a frequent but often under-diagnosed complication, especially after a major hip surgery. POD is according to DSM-5 is an acute onset of attention impairments with fluctuating levels of awareness and cognition over a period.

The incidence of delirium varies anywhere from 9 to 87%. Delirium although multi-factorial, often involves the presence of precipitating events in a high-risk individual. Postoperative recovery is often delayed in delirium patients adding to increased duration of hospital stay and financial burden, and in extreme cases, even an increased risk of mortality. The risk factors that have an associated with postoperative delirium are age diabetes, high American Society of Anesthesiologists (ASA) grading, electrolyte imbalance, and blood pressure fluctuations. The elderly population is at more risk for sustaining fractures around the hip and also for a high incidence of postoperative delirium. Malnutrition, being a modifiable risk factor, is extremely common in the elderly and could be an important aspect.

Optimizing control of diabetes and hypertension, correcting malnutrition, and identifying and treating osteoporosis go a long way in preventing fragility fractures, and thereby, POD. The role of the primary care physician in this scenario is invaluable. A detailed history, prompt timely identification, and intervention provide an opportunity to correct and modify risk factors, and hence, prevent the occurrence of POD.

**Methodology**

The present study was a cross-sectional observational one with the intent to treat the study done at a tertiary care setting in South India. Institutional ethical committee clearance was obtained.

The study included all patients aged more than 60 years of both genders presenting with hip fractures to our hospital from January 2020 to December 2021. Both intra- and extracapsular hip fractures were included in the study. Patients with the following conditions were excluded: (a) preoperative cognitive impairment, (b) polytrauma patients with head injury, (c) known psychiatric disorders, (d) patients with epilepsy and parkinsonism, and (e) patients with hepatic or renal impairment. Patients who were not willing to be a part of the study were also excluded from the study. Informed consent was taken from all the study participants.

A detailed history which included social-demographic parameters, clinical history, significant medical history, and drug usage (benzodiazepines, hypnotics, and diuretics) was collected. Information regarding the type of fracture, surgery planned, and anesthesia was also noted. The ASA grading was done as per the American Society of Anesthesiologists’ classification of Physical Health. The nutritional status assessment was done using the “Mini nutritional assessment” (MNA) scale. Based on the MNA scores, the patients were classified as a) normal nutrition: MNA score ≥24, b) at risk for malnutrition: MNA score 23-17, and c) overt malnutrition: MNA score less than 17.

Data regarding preoperative blood investigations like complete blood picture, serum albumin levels, blood sugars, glycosylated hemoglobin HbAlc levels, and serum electrolytes were noted.

**Surgical procedure**

After standard pre-anesthetic evaluation and physician consultation, patients underwent appropriate surgeries. Hemiarthroplasty was done for intracapsular fractures and extracapsular fractures were reduced and fixed using a dynamic hip screw (DHS) or proximal femoral nail (PFN). The surgical wound was closed in layers and the dressing was applied.

**Postoperative details**

All patients received standard postoperative care. Supervised joint range of motion exercises and physiotherapy were begun as early as the patient could tolerate. Postoperatively, all patients were screened for the onset of symptoms of delirium twice daily by a team of trained nurses and physicians as per the Confusion Assessment Method (CAM). Details regarding the duration of surgery, type of anesthesia, and postoperative blood values were also noted.

**Statistical analysis**

The data were entered into MS Excel 2007 version and analyzed using SPSS software. The categorical variables were analyzed by using percentages, and the continuous variables were analyzed by calculating the mean ± standard deviation. The t-test was planned for normal distribution. The Chi-squared test was used to determine the significance of categorical variables. A P value < 0.05 was considered statistically significant and a P value < 0.001 was considered highly significant. Univariate and multivariate analyses were done.

**Results and Observations**

A total of 137 patients presented with hip fractures during the study period. Twenty-seven patients (13 with head injury, 6 with seizure disorder, and 8 patients with chronic renal failure) were excluded from the study. One hundred and ten patients fulfilling the inclusion and exclusion criteria were admitted to the study. Among the one hundred and ten patients, forty-nine patients developed delirium [Table 1]. The incidence of delirium in the postoperative period was 44.54%. There was a statistical difference in the occurrence of POD for age (P = 0.014). The percentage of patients developing delirium was directly proportional to their advancing age [Chart 1]. There was male preponderance in both the non-delirium and delirium groups. Extracapsular hip fractures were more commonly seen in both groups (84 and 69%, respectively). There was no statistical difference in preoperative values of serum sodium, serum potassium, and serum chloride (P-values of 0.91, 0.971, and 0.117 respectively). The occurrence of postoperative delirium in diabetic patients as compared to non-diabetics was statistically significant (P-value 0.002). In hypertensive patients compared to non-hypertensive patients, the development of delirium
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was not significant ($P$-value 0.246). There was a statistically significant difference in the delirium group among malnourished, hypo-albuminemia, and uncontrolled diabetic patients ($P<0.001$ in all three groups).

### Univariate analysis interpretation

Logistic regression was performed to ascertain the effects of age, nutritional status (MNA), serum albumin levels, and HbA1c levels on the likelihood that participants develop delirium in the postoperative period.

As compared to a person who is 60 years old, a person aged more than 80 years is three times more likely to develop delirium which was statistically significant ($P = 0.017$). In comparison to a person with normal nutrition, patients in the malnourished group were 18 times more likely to develop delirium which was highly statistically significant ($P<0.001$). [Table 3] Patients presenting with hypoalbuminemia were 14 times more likely to develop delirium which was statistically significant ($P=0.001$). Similarly, patients who presented with uncontrolled diabetes ($HbA1c > 7.5$) were 33 times more likely to develop delirium compared to non-diabetic patients, which was statistically significant ($P < 0.001$).

### Multivariate analysis interpretation

Compared to a patient aged 60 years, a patient aged more than 81 was 1.112 times more likely to develop delirium after being adjusted for other variables which were statistically significant ($P = 0.034$). Compared to patients with normal nutritional status, patients in the malnourished group were 44 times more likely to develop delirium after adjusting for other variables and which was statistically significant ($P = 0.006$). Similar observations were seen in patients presenting with hypoalbuminemia (odds ratio-OR 147.218; 95% CI: 36.294 - 593.686).
confident interval CI 5.447–3978.828, P = 0.003). Patients presenting with uncontrolled diabetes (HbA1c > 7.5%) were 59 times as likely to develop delirium as compared to patients with normal serum albumin levels (OR 59.262, 95% CI 4.972–706.370; P = 0.001).

**Discussion**

The occurrence of delirium in the elderly in the postoperative period delays functional ability and rehabilitation. Although delirium has typically been perceived as a temporary, short-term illness, its indelible effects, morbidity, and increased monetary costs, including mortality, are unquestioned.

Delirium is frequently multi-factorial. It generally involves precipitating events in a high-risk or predisposed person. Information about these precipitating factors helps the treating team in the identification of high-risk individuals and employing measures to prevent the occurrence of delirium and timely management.

**Age**

As one ages, there is a decline in attention span. Delirium is a significant complication that prolongs hospitalization, delays recovery, and increases the burden on the patient’s family. The incidence of POD in this study was 44.54%. This ranges from 9 to 87% depending on the presence of the risk factors according to Mosk et al. Scholtens RM et al. reported an incidence of 13–48%. The incidence is highly variable on the criteria used for diagnosis and is different in these studies. Additionally, various factors like sample size, selection of patients’ surgical technique, and type of anesthesia may also influence the incidence. As CAM is one of the validated tools for the assessment of delirium, the same was used in this study to maintain precision and integrity.

The frequency of POD increases by 2% when the age of the patient increases by 1 year. The geriatric population is at more risk of sustaining hip fractures and also a high incidence of POD. In this study, out of 110 patients, 67 patients were between 60 and 70 years, 36 patients were between 71 and 80, and 7 patients above 81 years [Table 2]. There was a statistical difference in the occurrence of POD for age (P = 0.014). The percentage of patients developing POD kept increasing as age advanced (40.2% among 60–70 years to 71.42% in the patients aged more than 81 years) [Chart 1]

Wang et al. and Dyer et al. found a high incidence and consistent relationship between advanced age and POD. As age advances, impaired compensatory physiological mechanisms, alterations in the central neurotransmitters pathways, and altered blood pressure regulatory mechanisms predispose the geriatric population to delirium. The ability to adapt to the physical stress of surgery may also contribute to cerebral hypoperfusion.

**Gender**

The present study had 27 male and 22 female patients in the delirium group. Gender did not have any influence on the occurrence of POD in this study (P = 0.095). Similar findings were noted by Wang et al.

**Diabetes**

Poorly controlled diabetics are at risk of developing POD. Long-standing diabetes is generally associated with cognitive dysfunction due to altered glucose metabolism and the deposition of amyloid. These factors lead to a reduction in the number of capillaries, an increase in the thickness of the basement membrane making the brain tissue more susceptible to hypoxia when blood pressure drops due to surgery or anesthesia.

This study demonstrated a statistically significant association between diabetes and POD (P = 0.002). Binomial logistical regression also revealed that uncontrolled diabetic patients are at a higher risk of developing POD (OR 40.22; 95% CI 3.80–424.90; P = 0.002).

**Hypertension**

The incidence of POD was 34.69% in the hypertensive group versus 24.59% in the non-hypertensive patients (P = 0.246). Impaired cerebrovascular autoregulations due to changes in vascular stiffness and cerebrovascular reactivity in hypertensives have been assumed to be the cause of POD. In addition, hypotension over time is also a significant risk factor for POD epidural anesthesia and can lower blood pressure leading to cerebral hypoperfusion and POD.

**ASA**

The ASA status has been linked to a poor general condition and various comorbidities. In this study, there was no statistical difference among patients in the delirium group as compared to the non-delirium group (P = 0.366).

**Serum electrolytes**

The role of serum electrolytes on POD is controversial. Studies by Zhang et al. and Wang et al. found that electrolyte abnormalities were significantly related to POD. Caplan et al. did not find a significant association. In the present study, there was no significant association of POD with preoperative serum values of sodium, potassium, and chloride (P-values: 0.091, 0.971, and 0.117, respectively).

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### Table 2: Logistic regression analysis relating to outcome delirium with age- univariate analysis

| Variables       | Odds ratio (95% CI) | P     |
|-----------------|---------------------|-------|
| Age             |                     |       |
| 60-70 years (Ref) |                     |       |
| 71-80 years     | 1.326 (0.58-2.99)   | P=0.49|
| >81 years       | 3.704 (0.66-20.49)  | P=0.134|

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References:

1. Venkatakrishnaiah, et al.: Risk factors for postoperative delirium in geriatric hip fractures patients
2. Wang et al.
3. Mosk et al.
4. Scholtens RM et al.
5. Caplan et al.
Malnutrition is a usual association in the geriatric population with hip fractures. A study was done to assess the nutritional status and its outcomes in elderly patients with hip fractures by Malafarina V et al.\(^{[26]}\) and concluded that malnutrition is very common in the elderly with many comorbidities. It is linked to functional changes, which can be both a cause and result of fracture.

MNA was used in this study for nutritional assessment. The difference between the POD group and the non-delirium group for nutritional status was highly significant \((P < 0.001)\). Logistic regression performed showed that malnourished patients were at a significantly higher risk of developing POD \([Table 3]\).

Malnutrition is of great importance as it is a risk factor for the occurrence of hip fractures and delays the ability to achieve full functional capacity in patients with hip fractures.\(^{[26,27]}\)

However, in this study, low serum albumin was an independent risk factor for the development of POD \((P < 0.001)\). Patients presenting with hypoalbuminemia were 14 times more likely to develop delirium which was statistically significant \((P = 0.001)\).

Bohl et al.\(^{[28]}\) stated that there was increased mortality in hypoalbuminemic geriatric patients following hip fracture surgery. A relative change in serum albumin was a significant risk factor for POD in elderly patients following total joint arthroplasty.\(^{[28,29]}\) The association between low serum albumin and its association with POD can be explained based on the hypotheses that albumin acts as an antioxidant agent by trapping free oxygen radicals. In hypoalbuminemia, this defensive mechanism is hampered in the central nervous system giving rise to toxic cognitive impairment.\(^{[30]}\)

To summarize, fragility fractures and postoperative delirium in the elderly are a cause of morbidity and mortality. Treatment of osteoporosis in the elderly cannot be overemphasized in preventing fragility fractures. As age is a non-modifiable risk factor, aligning one's preventive goals toward prompt and early identification and treatment of modifiable risk factors like malnutrition, serum protein levels, optimizing blood sugars, and control of hypertension go a long way in preventing POD. Since primary care and family physicians form the first contact for this subset of patients, a thorough working knowledge of delirium, identification and management of its causes are very essential. Primary prevention strategies aimed at risk factor modification save time, energy, and money for all the stakeholders.

### Conclusion

Postoperative delirium is associated with risk factors that are modifiable and non-modifiable. Advancing age, hypoalbuminemia, malnourishment, and uncontrolled diabetes are strong predictors for the development of postoperative delirium in geriatric hip fracture patients. Since age is a non-modifiable risk factor, interventional strategies aimed at correcting modifiable risk factors like nutrition, serum albumin levels, and diabetes control play an important part in preventing delirium in the postoperative period in elderly hip fracture patients. Perioperative risk reduction would be the most appropriate approach to managing postoperative delirium.

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### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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### Table 3: Logistic regression analysis relating to outcome delirium with age, nutritional assessment (MNA), serum albumin levels, and diabetes (HbA1c levels)

| Variables                          | Unadjusted Odds ratio (95% CI) | P   | Adjusted Odds ratio (95% CI) | P   |
|------------------------------------|--------------------------------|-----|------------------------------|-----|
| **Age**                            |                                |     |                              |     |
| MNA<sup>1</sup>- Normal nutritional status (Ref) |                                |     |                              |     |
| At risk of malnutrition            | 1.34 (0.48-3.74)               | 0.572 | 1.244 (0.277-5.578)          | 0.776 |
| Malnourished                       | 18.13 (3.56-92.12)             | 0.000 | 44.734 (3.820-523.865)       | 0.002 |
| Serum Albumin 3.5-5 g/dl (Ref)     | 14.224 (3.15-64.18)            | 0.001 | 147.218 (5.447-3978.828)     | 0.003 |
| <6.5%                               |                                |     |                              |     |
| Glycosylated hemoglobin-HbA1c      |                                |     |                              |     |
| 6.5%-7.5%                          |                                |     |                              |     |
| >7.5%                              |                                |     |                              |     |

\(^{1}\)MNA-Mini nutritional assessment scale
References

1. Cooper C, Campion G, Melton LJ 3rd. Hip fractures in the elderly: A world-wide projection. Osteoporos Int 1992;2:285-8.

2. Chrispal A, Mathews KP, Surekha V. Clinical profile and association of delirium in geriatric patients with hip fractures in a tertiary care hospital in India. J Assoc Physicians India 2010;58:15-9.

3. Thom RP, Levy-Carrick NC, Bui M, Silbersweig D. Delirium. Am J Psychiatry 2019;176:785-93.

4. Mosk CA, Mus M, Vroemen JP, van der Ploeg T, Vos DI, Trabold B, Metterlein T. Postoperative delirium: Risk factors, prevention, and treatment. J Cardiothoracic Vasc Anesthesia 2014;28:1352-60.

5. Dyer CB, Ashton CM, Teasdale TA. Postoperative delirium. A review of 80 primary data-collection studies. Arch Intern Med 1995;155:461-5.

6. Smith TO, Cooper A, Peryer G, Griffiths R, Fox C, Cross J. Delirium and risk factors of postoperative delirium in elderly hip fracture patients. Clin Interv Aging 2017;12:421-30.

7. Vellas B, Villars H, Abellan G, Soto ME, Rolland Y, Guigoz Y, Irnius A, Edlund A, Lundström M, Brännström B, Bucht G, Peris A, Kong S, Wang J, Xu H, Wang K. Effect of hypertension and medication use regularity on postoperative delirium after maxillofacial tumors radical surgery. Oncotarget 2015;12:1811-20.

8. Smith TO, Cooper A, Peryer G, Griffiths R, Fox C, Cross J. Factors predicting incidence of post-operative delirium in older people following hip fracture surgery: A systematic review and meta-analysis. Int J Geriatr Psychiatry 2017;32:386-96.

9. Ringaitiene D, Gineityte D, Vicka V, Žvirblis T, Šipylaitė J, Irmius A, et al. Impact of malnutrition on postoperative delirium development after on pump coronary artery bypass grafting. J Cardiothorac Surg 2015;10:74.

10. Li S, Zhang J, Zheng H, Wang X, Liu Z, Sun T. Prognostic role of serum albumin, total lymphocyte count, and mini nutritional assessment on outcomes after geriatric hip fracture surgery: A meta-analysis and systematic review. J Arthroplasty 2019;34:1287-96.

11. Guo Y, Jia P, Zhang J, Wang X, Jiang H, Jiang W. Prevalence and risk factors of postoperative delirium in elderly hip fracture patients. J Int Med Res 2016;44:317-27.

12. Vellas B, Villars H, Abellan G, Soto ME, Rolland Y, Guigoz Y, Irnius A, Edlund A, Lundström M, Brännström B, Bucht G, Peris A, Kong S, Wang J, Xu H, Wang K. Effect of hypertension and medication use regularity on postoperative delirium after maxillofacial tumors radical surgery. Oncotarget 2015;12:1811-20.

13. Edlund A, Lundström M, Brännström B, Bucht G, Gustafson Y. Delirium before and after operation for femoral neck fracture. J Am Geriatr Soc 2001;49:1335-40.

14. Malafarina V, Reginster JY, Cabrerizo S, Bruyère O, Kanis JA, Martinez JA, et al. Nutritional status and nutritional treatment are related to outcomes and mortality in older adults with hip fracture. Nutrients 2018;10:555.

15. Helminen H, Luukkaala T, Saarnio J, Nuotio M, Rotter I. Diabetes and elevated preoperative HbA1c level as risk factors for postoperative delirium after cardiac surgery: An observational cohort study. Neuropsychiatr Dis Treat 2019;15:511-21.

16. Bohl DD, Shen MR, Hannon CP, Fillingham YA, Darrith B, Della Valle CJ. Serum albumin predicts survival and postoperative course following surgery for geriatric hip fracture. J Bone Joint Surg Am 2017;99:2110-8.

17. Qi J, Liu C, Chen L, Chen J. Postoperative serum albumin decrease independently predicts delirium in the elderly subjects after total joint arthroplasty. Curr Pharm Des 2020;26:386-94.

18. Llewellyn DJ, Langa KM, Friedland RP, Lang IA. Serum albumin concentration and cognitive impairment. Curr Alzheimer Res 2010;7:91-6.