## RESEARCH ARTICLE

# Pre-operative Anemia and Hyponatremia Increase the Risk of Mortality in Elderly Hip Fractures

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### Abstract

**Objectives:** Pre-operative assessment is routinely performed for all hip fractures, and include a thorough clinical examination and multiple pre-operative tests. While abnormalities are often detected in many tests, they have varied effect on mortality. The purpose of the study was to assess the prevalence and impact of these abnormal tests and comorbidities.

**Methods:** This was a prospective study of 283 consecutive hip fracture patients aged above 50 years admitted in a major trauma hospital from February 2019 to December 2019. The prevalence of abnormalities in the following tests were assessed: chest x-ray, electrocardiogram, complete blood count, serum electrolytes, renal function test, prothrombin time/international normalized ratio, and serum bilirubin. Also, presence of comorbidities were recorded. Mortality within 90 days of admission was assessed.

**Results:** 91.5% (N= 259/283) of the patients had at least one abnormal investigation. The most common abnormal investigation was anemia (70.3%, N= 199/283), followed by deranged sodium (36.4%, N= 103/283). 17.7% (N= 50/283) of the patients had at least one new comorbidity diagnosed after admission. The most common newly diagnosed comorbidity was hypertension (10.6%, N= 30/283). Anemia (p=0.044), deranged sodium (p=0.002), raised urea (p=0.018), raised creatinine (p=0.002), renal disease (p=0.015), neurological diseases (p=0.024), and charlson comorbidity index (p=0.004) were associated with increased mortality in multivariate analysis.

**Conclusion:** Pre-operative hemoglobin, sodium, urea, and creatinine were the most important tests influencing mortality, and derangements of these should therefore be carefully evaluated and managed. Hip fracture care pathways should focus on correction of these abnormalities.

Level of evidence: II

Keywords: Comorbidities, Hip fracture, Mortality, Preoperative tests

### Introduction

bout 50-70% of the elderly patients suffering from hip fractures have at least one comorbidity.<sup>1,2</sup> Unfortunately, many comorbidities in the elderly population are not diagnosed in a timely manner and are inappropriately managed as many of these illnesses can be silent.<sup>3,4</sup> Also, about one in six of the elderly population in the world experience psychological abuse.<sup>5</sup> This can hinder appropriate management of their comorbidities, especially in low-income countries where they have to depend on the younger earning members of the family for regular physician visits.<sup>6,7</sup> Hip fracture is an acute debilitating event, and patients invariably seek medical attention. As

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surgery is the preferred treatment for these patients, they undergo a detailed medical evaluation involving a number of pre-operative tests which often reveal many abnormalities.<sup>8</sup> In addition to the already known comorbidities, such newly detected medical ailments might have an effect on the outcomes of these patients.<sup>9-11</sup>

The one-year mortality after hip fractures is estimated to be about 30%.<sup>12-14</sup> Medical comorbidities and frailty of these patients are thought to be primarily responsible for such a high mortality.<sup>2,15</sup> As there is a general tendency to operate hip fractures on an urgent basis, there are concerns on the utility of the various pre-operative tests which may



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delay surgery, and may not actually alter the treatment plan.<sup>16</sup> Therefore, it is important to identify the extent to which abnormalities are detected in the pre-operative tests, and to understand whether they have an impact on mortality. Also, all comorbidities and abnormal lab results may not have the same effect on outcomes. Understanding the medical conditions responsible for higher mortality will help in identifying the high-risk patients at the time of admission who may require a different care pathway.

Therefore, the current study was conducted to assess: 1) the prevalence of abnormal results in routine pre-operative tests, and the prevalence of comorbidities among elderly Indian hip fractures; and 2) the impact of the various abnormal test results and comorbidities on 90-day mortality.

#### **Materials and Methods**

The study was commenced after obtaining approval from the Institution Ethical Committee. Patients were included in the study after written informed consent. This was a prospective observational study of consecutive elderly hip fracture patients admitted at a single tertiary level trauma center from February, 2019 to December, 2019. Data was collected by in-person interview of the patient and/or relatives at the time of admission along with review of their medical records.

All hip fractures (proximal femur fractures: neck, intertrochanteric, or subtrochanteric) above 50 years were included in the study. During the study period, there were 377 hip fracture admissions of which 93 were under the age of 50. One patient did not give consent, and was not included, Therefore, a total of 283 patients who were included in the study. The mean age of the cohort was  $70\pm12$  years, and there were 152 (54%) females. Intertrochanteric fractures were the most common fracture type (N=182, 64%) followed by neck of femur (N=77, 27%), and subtrochanteric fractures (N=24, 9%). All patients presented to the emergency department, and were attended by an orthopedic surgeon. Pre-operative assessment was conducted by the anesthetic team which included an appropriate medical examination and review of the (CXR), following routine tests: chest x-rav electrocardiogram (ECG), complete blood count, serum function prothrombin electrolytes, renal test, time/international normalized ratio (INR) and serum bilirubin. Surgery was planned for the earliest available slot provided the patient was fit for surgery based on the anesthetist's assessment. Patients who needed preoperative optimization (such as correction of anemia, correction of serum electrolytes, control of blood sugars or blood pressure, etc.) were accordingly managed by interdisciplinary team involving orthopedic surgeons, geriatric physicians, and other specialists as required. After surgery (fixation or replacement), patients were mobilized on day 1 and were discharged by day 2 or 3 if the wound was healthy.

Comorbidities included in the charlson comorbidity index (CCI) were assessed.<sup>17</sup> These included history of myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, peptic ulcer disease, liver disease (mild, moderate or severe), diabetes ABNORMAL PREOPERATIVE TESTS AND COMORBIDITIES IN ELDERLY INDIAN HIP FRACTURES

(uncomplicated or with end organ damage), hemiplegia, renal disease (moderate or severe), tumor, lymphoma, leukemia, metastasis, and AIDS.<sup>17</sup> Based on these comorbidities, both CCI (score ranging from 0 to 33) and age-adjusted CCI (score ranging from 0 to 37) were calculated. Additionally, the following comorbidities which were not a part of CCI were assessed: hypertension, hypothyroidism, other neurological disease, psychoses, depression, cardiac arrythmia, and valvular disorders. The presence of any of these comorbidities at admission was obtained through history from patients or relatives, or using their previous medical records or during evaluation after admission by the orthopedic/anesthetic team and/or other specialists.

The lab tests performed at the time of admission were recorded. For the purposes of study, the results of ECG and CXR as interpreted by the anesthetist (or cardiologist or pulmonologist when available) were recorded as normal or abnormal. Anemia was defined based on the world health organization (WHO) definition as hemoglobin (Hb) <13 g/dL in men and Hb <12 g/dL in women.<sup>18</sup> Severe anemia was defined as Hb < 8 g/dL.<sup>18</sup> Thrombocytopenia was defined as platelet count < 150,000 per  $\mu$ L. The normal ranges for total leukocyte count (TLC) and INR were taken as 4000-11000 per  $\mu$ L and 0.9-1.1 respectively, with anything beyond this range considered as abnormal. Raised urea, creatinine, and bilirubin were defined using the following cut-offs respectively: >48 mg/dL, > 1.2 mg/dL, and > 1.2 mg/dL. The normal ranges used for sodium and potassium were 135-145 mEq/L and 3.5-5.1 mEq/L respectively.

All patients were followed up to assess all-cause mortality within 90 days of the admission. Patients who were not operated or died before surgery were also included in this study. Surgery was performed in 96.8% (N=274/283) patients (total hip arthroplasty=8 [all uncemented], hemiarthroplasty=49 [22-cemented], fixation=215 [cephalomedulary nail=196, cannulated cancellous screw=14, dynamic hip screw=4, blade plate =1); 2 patients decided to get operated outside our institution and the details were not available). The choice of fixation was based on surgeon's choice. The post-operative DVT prophylaxis at our hospital consisted of mechanical prophylaxis and tablet Aspirin 75 mg once a day for 28 days. Four patients died before surgery (1-pneumonia, 1-renal failure, 1- arrythmia, 1- stroke), two refused surgery and left against medical advice, and the remaining three were managed conservatively in view of poor health. Data regarding the death was obtained through medical records (during admission or re-admission) or by telephone interview of the patients' relatives.

Categorical variables were compared using a Chi-squared or Fisher Exact test. Students t-test sum was used to compare continuous variables. A univariate logistic regression was used to assess the factors associated with mortality. A multivariate logistic regression model was used to study the association between individual variables and mortality after adjusting for age, gender, and type of fracture. As the number of newly diagnosed comorbidities were low, both newly diagnosed and previously diagnosed comorbidities were considered together when studying the association between each of these comorbidities and mortality. The level of significance for rest of the analysis THE ARCHIVES OF BONE AND JOINT SURGERY. ABJS.MUMS.AC.IR ABNORM VOLUME 12. NUMBER 5. May 2024 ELDERL

> was also set at p < 0.05. Statistical analysis was completed using Stata statistical software, version 12 (StataCorp, College Station, TX).

#### **Results**

91.5% (N= 259/283) of the patients had at least one abnormal investigation. The most common abnormal investigation was anemia (70.3%, N= 199/283), followed by deranged sodium (36.4%, N= 103/283) [Table 1]. Overall, 68.9% (N=195/283) of the patients had at least

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one comorbidity with the most common one being hypertension (45.9%, N= 130/283) followed by uncomplicated diabetes (19.8%, N= 56/283) [Table 2]. The mean CCI score was  $0.75 \pm 1.07$  (range, 0 to 6) while the age adjusted CCI score was  $3.14 \pm 1.53$  (range, 0 to 8). The CCI score was higher, but not statistically significant in those with a new comorbidity ( $1.00 \pm 1.2$  vs  $0.70 \pm 1.06$ , p=0.074), as was age adjusted CCI score ( $3.67 \pm 1.35$  vs  $3.01 \pm 1.56$ , p=0.079).

Table 1. Prevalence of abnormal investigation reports	
Investigation	Number (%)
Any abnormal investigation	259 (91.5%)
Anemia (<12 g/dl in females, <13 g/dl males)	199 (70.32%)
Severe anemia (< 8 g/dl)	22 (7.77%)
Abnormal TLC (<4000 per μL,>11000 per μL)	47 (16.61%)
Thrombocytopenia (<150 per μL)	77 (27.21%)
Abnormal INR (<0.9,>1.1)	62 (21.91%)
Deranged sodium (<135 mEq/L, >145 mEq/L)	103 (36.4%)
Deranged potassium (<3.5 mEq/L, >5.1 mEq/L)	35 (12.37%)
Raised Urea (>48 mg/dL)	60 (21.2%)
Raised Creatinine (>1.2 mg/dL)	37 (13.07%)
Raised Bilirubin (>1.2 mg/dL)	35 (12.37%)
Abnormal ECG	91 (32.16%)
Abnormal CXR	46 (16.25%)

Table 2. Prevalence of comorbidities	
Comorbidity	N (%)
Hypertension	130 (45.94%)
Uncomplicated diabetes	56 (19.79%)
Chronic lung disease	32 (11.31%)
Cerebrovascular accident	22 (7.77%)
Hypothyroidism	13 (4.59%)
Other neurological diseases	10 (3.53%)
Complicated Diabetes	9 (3.18%)
Tumor	9 (3.18%)
Dementia	8 (2.83%)
Moderate or severe renal disease	8 (2.83%)
Cardiac arrhythmia	8 (2.83%)
Congestive Heart Failure	6 (2.12%)
Connective tissue disease	6 (2.12%)
Myocardial infarction	5 (1.77%)
Hemiplegia	4 (1.41%)
Psychoses	3 (1.06%)
Depression	3 (1.06%)
Peptic ulcer disease	2 (0.71%)
Metastasis	2 (0.71%)
Valvular disease	2 (0.71%)
Chronic liver disease	2 (0.71%)

Follow-up was available for 97.2% (N=275/283) patients at 90-days. Out of these, 9.8% (N=27/275) patients died. The in-hospital mortality was 2.5% (7/283). Seven (2.5%) patients had a re-operation (3- implant failure, 2-infection, 1- dislocation, 1- periprosthetic fracture), Mortality among patients with re-operation was 14.3% (N=1/7) while it was 9.7% (N=26/268) among those without reoperation, p=0.519. Among the abnormal investigations, anemia (p=0.017), severe anemia (p=0.042), deranged sodium (p=0.017), raised urea (p=0.003) and raised creatinine (p<0.001) were associated with increased mortality. Anemia (p=0.018) and raised creatinine (p=0.002) were also associated with increased mortality in multivariate analysis [Table 3]. All patients who died had at least one abnormal investigation, and hence, odds ratio was not calculated. On

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univariate analysis, presence of any comorbidity (p=0.016), CCI score (p=0.006) and age adjusted CCI (p=0.037) were associated with increased mortality [Table 4]. Individually, moderate or severe renal disease (p=0.018) and other neurological diseases (p=0.043) were associated with increased mortality. On multivariate analysis, presence of any comorbidity (p=0.026), CCI score (p=0.004), age adjusted CCI (p=0.043), moderate or severe renal disease (p=0.015) and other neurological diseases (p=0.024) were associated with increased mortality [Table 4]. The odds ratio for the following comorbidities were not calculated due to lack of events (mortality) in either of the groups (comorbidity present/absent): myocardial infarction, connective tissue disease, peptic ulcer disease, chronic liver diseases, hypothyroidism, psychoses and valvular diseases.

Table 3. Influence of abnormal investigations on 90-day mortality					
Investigation	Odds ratio (95% CI)	P-value	Adjusted odds ratio (95% CI)	P-value	
Anemia	5.95 (1.38-25.75)	0.017	4.60 (1.04-20.38)	0.044	
Severe anemia	3.09 (1.04-9.17)	0.042	2.67 (0.86-8.26)	0.089	
Abnormal TLC	0.36 (0.08-1.58)	0.176	0.34(0.07-1.51)	0.155	
Thrombocytopenia	0.93(0.37-2.29)	0.869	1.05 (0.41-2.66)	0.922	
Abnormal INR	1.26(0.51-3.13)	0.623	1.27(0.50-3.25)	0.613	
Deranged sodium	4.72 (1.98-11.23)	< 0.001	3.98 (1.64-9.68)	0.002	
Deranged potassium	1.22(0.39-3.76)	0.732	1.13(0.35-3.63)	0.841	
Raised Urea	3.51 (1.54-8.01)	0.003	2.90(1.20-7.00)	0.018	
Raised Creatinine	4.81 (2.00-11.57)	< 0.001	4.94(1.84-13.27)	0.002	
Raised Bilirubin	0.25 (0.03-1.90)	0.182	0.33 (0.04-2.60)	0.294	
Abnormal ECG	1.50(0.66-3.38)	0.330	1.15(0.49-2.71)	0.744	
Abnormal CXR	2.40 (0.98-5.89)	0.056	2.27(0.89-5.82)	0.087	

CI- Confidence Interval, TLC- Total Leukocyte Count, INR- International Normalized Ration, ECG-electrocardiogram, CXR- Chest X-ray

Table 4. Influence of comorbidities on 90-day mortality					
Comorbidity	Odds ratio (95% CI)	P-value	Adjusted odds ratio (95% CI)	P-value	
Any comorbidity	6.06 (1.40-26.22)	0.016	5.45 (1.22-24.02)	0.026	
CCI score	1.50(1.13-2.01)	0.006	1.61 (1.16-2.21)	0.004	
Age-adjusted CCI*	1.71(1.03-2.84)	0.037	1.68 (1.02-2.78)	0.043	
Number of comorbidities					
0	Ref		Ref		
1	5.37 (1.15-24.97)	0.032	4.86 (1.01-23-34)	0.048	
2	7.10 (1.50-33.66)	0.013	6.41(1.31-31.33)	0.022	
>2	5.99 (1.04-34.60)	0.045	5.21 (0.87-31.14)	0.070	
Hypertension	1.49(0.67-3.32)	0.325	1.27(0.55-2.93)	0.575	
Uncomplicated diabetes	1.19(0.45-3.11)	0.722	1.25(0.46-3.39)	0.667	
Chronic lung disease	1.94 (0.68-5.55)	0.217	1.87(0.63-5.57)	0.263	
Cerebrovascular accident	1.59 (0.44-5.81)	0.478	1.37 (0.35-5.34)	0.648	
Other neurological diseases	4.30 (1.04-17.73)	0.043	5.84(1.26-27.13)	0.024	
Complicated Diabetes	2.75 (0.54-13.98)	0.222	3.14 (0.58-16.98)	0.184	
Tumour	1.15 (0.14-9.60)	0.895	1.16 (0.13-10.28)	0.893	

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Table 4. Continued				
Dementia	1.32 (0.16-11.19)	0.796	1.02(0.11-9.21)	0.984
Moderate or severe renal disease	6.08(1.37-26.99)	0.018	7.74(1.48-40.39)	0.015
Cardiac arrythmia	3.23(0.62-16.84)	0.165	2.83(0.46-17.41)	0.261
Congestive Heart Failure	1.87(0.21-16.61)	0.575	2.58(0.27-24.82)	0.411
Hemiplegia	3.14 (0.32-31.29)	0.329	3.64(0.31-42.31)	0.303
Depression	4.73(0.41-53.96)	0.211	4.21(0.33-53.64)	0.269
Metastasis	9.5 (0.57-156.39)	0.115	13.82 (0.74-258.67)	0.079

\*For age-adjusted CCI, age was not included in the multivariate analysis reporting adjusted odds ratio. CI- Confidence Interval, CCI- Charlson Comorbidity Index

#### **Discussion**

Surgery is the preferred treatment for hip fractures, and all patients undergo a pre-operative medical assessment which often reveals multiple abnormalities. In this study, we assessed the prevalence of abnormal lab investigations and comorbidities in a consecutive series of hip fractures. Our study found that 92% of the hip fracture patients had at least one abnormality in the routine lab investigations. Overall, 69% of the patients had at least one comorbidity. Anemia was the most commonly detected lab abnormality while hypertension was most commonly diagnosed comorbidity. Our study also found that anemia, deranged sodium, raised urea, and raised creatinine were associated with increased mortality. Although composite measures of comorbidity like CCI and the presence of comorbidities in general increased the risk of mortality, commonly detected comorbidities such as hypertension and diabetes were not associated with a higher risk of mortality.

The vast majority of the patients had at least one abnormality in the routinely performed tests. Anemia was the most commonly detected lab abnormality followed by deranged sodium level, and both of these were associated with higher mortality. Other studies have also found a strong relationship between anemia and mortality after hip fractures.<sup>10,19,20</sup> Interestingly, though severe anemia was found to be associated with increased mortality in univariate analysis, it was not associated with mortality after adjusting for confounders suggesting that severe anemia may not have a strong association as anemia. This might be because, patients with severe anemia are often closely monitored and almost always receive transfusions pre-operatively which lead to an improvement in the Hb.18 This suggests that patients at borderline anemia might be at higher risk of mortality as their anemia may not always be adequately addressed. The in-hospital and 90-day mortalities in our studies were 2.5% and 9.8% respectively, which were comparable to other studies.<sup>11,21</sup> The prevalence of deranged sodium (36%) in the study was slightly larger than that reported in other studies (20-25%),<sup>9,21-24</sup> though other studies also reported consistently higher mortality with deranged sodium. <sup>9,21,23,24</sup> As some studies have shown that hyponatremia is associated with increased risk of hip fractures, independent of bone mineral density, it is possible that many of the hip fracture patients may have had derangements in blood sodium even before the injury. <sup>25,26</sup> Although severe hyponatremia is usually corrected, orthopaedic surgeons should also be aware about mild abnormalities which can easily be overlooked.<sup>23</sup>

Overall, hypertension was the most prevalent comorbidity (46%). Hypertension was also the most prevalent comorbidity in the studies by Penrod et al., <sup>27</sup> Dhibar et al.<sup>28</sup> and, Reig et al.<sup>11</sup> conducted in United States, India, and Spain respectively. But hypertension which was not found to be associated with mortality similar to other studies.<sup>29,30</sup> Also, hypertension is not a part of the commonly used CCI which has been shown to be a better predictor for poor outcomes in various studies.<sup>31-33</sup> Elevations in either urea or creatinine were associated with increased mortality in our study similar to the findings by Jonsson et al.<sup>19</sup> and Seyedi et al.<sup>34</sup> Elevated serum creatinine may pre-dispose patients to acute kidney injury in the peri-operative period which has been shown to increase mortality.<sup>35,36</sup> Raised urea may be a sign of poor hydration suggesting that these patients might need better management and monitoring of their fluid intake and output.<sup>37</sup> Although we did not classify patients based on severity, diabetes was not associated with increased mortality suggesting that unnecessary delay in surgery awaiting optimization of sugars maybe avoided.

The study has a number of limitations. The sample size is only moderately sized, and a number of comorbidities which failed to show an association with mortality might have been significantly associated with mortality if the sample size was larger. However, this study included a consecutive series of hip fractures, and thus also included patients who did not underwent a surgery due to medical reasons, resulting in a more accurate estimation of the prevalence of abnormal tests and comorbidities. The present study only assessed those investigations which were routinely performed at our institution as part of the pre-operative assessment. However, other lab parameters might also have an influence on outcomes, and some of them might be routinely performed at other centres. Also, the abnormal results were based on ranges used in our laboratory, and there might be some variations in the normal ranges depending on the country and laboratory, although these changes are unlikely to affect the conclusions of the study. Also multiple other medical conditions such as obesity, drug abuse, smoking, etc which are not part of the Charlson Comorbidity Index were not included in the study and may influence mortality.<sup>17</sup>

#### Conclusion

patients had an abnormal investigation with the most frequently detected abnormalities being anemia and deranged sodium. Pre-operative Hb, sodium, urea and creatinine were the most important tests influencing mortality, and derangements of these should therefore be carefully evaluated and managed. In general, presence of comorbidities increased the risk of mortality though different comorbidities had varied effects. Presence of a renal disease or neurological disease were associated with higher risk of mortality while common comorbidities such as hypertension and diabetes did not show an association with mortality. The findings of our study is helpful in developing hip fracture care pathways aimed at correction of abnormalities which have a substantial effect on mortality.

#### **Acknowledgement**

Not applicable

In summary, about nine out of every ten hip fracture

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