



# Assessing the Frequency Investigation and Management of Post-Operative Anaemia in Hip Fracture Patients

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## ABSTRACT

**Background:** Post-operative anaemia affects up to 90% of patients undergoing major surgery. Post-operative anaemia can contribute to slower rehabilitation, increased morbidity, and increased mortality.

**Purpose:** We aimed to examine the frequency, investigation, and management of anaemia in patients admitted to an Irish, tertiary level hospital (SVUH) with a hip fracture.

**Methods:** A retrospective audit, examining all patients who were admitted to SVUH with a hip fracture between the 1<sup>st</sup> of April and the 30<sup>th</sup> of June 2020, was performed.

**Results:** A total of 58 patients were included. Upon admission, 29.3% (n=17) of patients were anaemic. Post-operatively, 91.4% of patients (n=53) were anaemic, 43.1% (n=25) of patients had iron studies, ferritin, folate and B12 levels measured. Iron deficiency anaemia was detected in 22.4% (n=13) of patients, folate deficiency was detected in 10.3% (n=6), and no patients were found to have vitamin B12 deficiency. Of the patients with iron deficiency anaemia, 15.4% (n=2) were given IV iron infusions and 7.7% (n=1) received a prescription for oral iron. Of the 6 patients with folate deficiency, 33.3% (n=2) received a prescription for folic acid. Red cell transfusions were given to 13.8% (n=8) of patients. Upon discharge, 89.7% (n=52) of patients remained anaemic.

**Conclusions:** Anaemia is an under-investigated and under-treated complication of hip fractures.

**Keywords:** Anaemia; Hip fractures; Ireland; Iron; Vitamin B12

## INTRODUCTION

The incidence of hip fractures in Ireland is rising [1-3]. This is largely a consequence of our aging population. In 2019, there were 3,701 recorded hip fractures in Ireland [4]. The median age of these patients was 80 for males and 82 for females [4]. As the national median age rises with each passing decade, increasing numbers of hip fractures are inevitable. A 2009 study found that annual hip fracture numbers are expected to increase by 100% by the year 2026 [3]. Despite advances in surgical and anaesthetic techniques, the mortality rate 1 year after hip fracture surgery remains between 15%-36% [5].

Numerous studies have found that anaemia on admission is an independent risk factor for mortality [6]. Additionally, post-operative anaemia is associated with increased morbidity, and

delayed recovery [7,8]. Despite the frequency of anaemia amongst hip fracture patients, there is a relative lack of literature on the subject. The frequency of anaemia upon admission to hospital with a hip fracture has been reported as being between 30%-45% [9]. The frequency of post-operative anaemia amongst these patients has been reported as being between 74%-86% [7,10].

The aetiology of anaemia amongst elderly hip fracture patients is multifactorial. Poor nutrition, chronic disease and a decreased haematopoietic reserve can lower the threshold for anaemia development in the context of blood loss. It has been estimated that 20% of females in the community aged between 80-85 are anaemic [9]. These individuals make up a significant proportion of hip fracture patients. Anaemia, as well as being a sign of frailty, also increases the risk of falls [11]. It is therefore both a risk factor for and a consequence of hip fractures. Intravenous

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**Received:** 20-May-2022, Manuscript No. JBBDT-22-16747; **Editor assigned:** 23-May-2022, Pre QC No. JBBDT-22-16747 (PQ); **Reviewed:** 06-Jun-2022, QC No JBBDT-22-16747; **Revised:** 13-Jun-2022, Manuscript No. JBBDT-22-16747 (R); **Published:** 20-Jun-2022, DOI: 10.35248/2155-9864.22.13.503.

**Citation:** McCormack D, Costigan O, McGarry E, O'Hanlon S, Hurson C (2022) Assessing the Frequency Investigation and Management of Post-Operative Anaemia in Hip Fracture Patients. J Blood Disord Transfus. 13:503.

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(IV) fluids and intra-operative blood loss can further contribute to the development of anaemia amongst hip fracture patients. Additionally, the metabolic response to surgery can result in a humoral suppression of erythropoiesis resulting in a functional iron deficiency [9].

The liver peptide hormone hepcidin is integral to the bioavailability of serum iron *via* the hepcidin/ferroportin axis [12]. Hepcidin reduces iron entry into plasma from absorptive duodenal cells and inhibits iron recycling macrophages by blocking iron export. It is stimulated by circulating inflammatory cytokines post-operatively including IL-6, TNF- $\alpha$  and IL-1 $\beta$  [13]. For this reason, oral iron supplementation has not been found to be useful in the management of post-operative anaemia in hip fracture patients [14]. The evidence for red cell transfusions in post-operative hip fracture patients is mixed and current guidelines recommend the use of restrictive transfusion criteria [15]. Some studies have found that transfusion improves mobility [7]. However, a North American trial comparing liberal vs. restrictive transfusion criteria in hip fracture patients found no difference in self-reported mobility or 60-day mortality [16]. Other studies have shown that although transfusion improves hemoglobin levels it is associated with increased rates of nosocomial infection [17]. Intertrochanteric and sub trochanteric fractures are the hip fracture types with the highest transfusion rates [9].

Intravenous iron treatment in hip fracture patients is recommended for the treatment of iron deficiency anaemia in post-operative patients [15]. IV iron does not have the same problems of absorption as oral iron in post-operative patients and has a lower rate of transfusion related side effects than RBC transfusion [9]. A Spanish randomized controlled trial conducted in 2005, showed that in certain subgroups peri-operative iron infusions decrease the requirements for later RBC transfusion and reduce rates of nosocomial infections [18]. A recent US study has shown that the use of IV iron decreases length of hospital stay and readmission rates in hip fracture patients [19]. However, there is a need for further research in this area. Given the ubiquity of anaemia in hip fracture patients, we sought to gain an insight into the frequency, investigation, and management of anaemia in an Irish tertiary level hospital.

## METHODOLOGY

A retrospective audit was carried out for all patients who were admitted to SVUH with a hip fracture between the 1<sup>st</sup> of April and the 30<sup>th</sup> of June 2020. We defined anaemia, in accordance with SVUH reference ranges, as a Haemoglobin level of <11.5 g/dL in Women and <13 g/dL in Men. Similarly, we used in hospital reference ranges to define folate and vitamin B12 deficiency. We used the association of anaesthetists' international consensus statement on the management of postoperative anaemia after major surgical procedures to set our parameters for iron deficiency. We established haemoglobin levels on admission, post operatively and on discharge, using the hospital's laboratory reporting system. Post-operative anaemia was measured on the third post-operative day, or if unavailable, on the day closest to day 3, (mean Day 2.96, range day 2-5). We ascertained whether iron studies, B12, Folate and Ferritin levels

were investigated during admission using the same reporting system. To establish whether patients had been transfused during their admission, we used the hospital's laboratory reporting system in conjunction with patient discharge letters. We reviewed discharge prescriptions and discharge summaries to establish whether patients received IV iron infusions during their admission and whether they were discharged with iron, folate or B12 supplementation.

## RESULTS

### Patient demographics and exclusions

A total of 66 patients presented to SVUH with a hip fracture between April 1<sup>st</sup> 2020 and June 30<sup>th</sup> 2020. Of this total, 71% (n=47) of patients were female and 29% of patients (n=19) were male. The mean age of patients on admission was 82 years old (range 61-101). From the overall total of 66 patients, 8 patients were excluded. There were 5 mortalities, (3f, 2m). We did not have access to the necessary documentation to include a further 3 patients (2f, 1m). This gave us a revised total of 58 patients (42f, 16m).

### Overview of results

Of the 58 patients included in this study, 29.3% (n=17) were anaemic upon admission. Post-operatively, 91.3% of patients (n=53) were anaemic. Of the total number of patients included in this study, 43.1% (n=25) had iron studies, ferritin, folate and B12 levels measured during their admission. Iron deficiency anaemia was detected in 22.4% (n=13) of patients, folate deficiency was detected in 10.3% (n=6), and no patients were found to have vitamin B12 deficiency. Of the 13 patients who were found to be iron deficient, 15.4% (n=2) were treated with IV iron infusions and 7.7% (n=1) were discharged with a prescription for oral iron. Of the 6 patients found to have folate deficiency, 33.3% (n=2) were discharged with a prescription for folic acid. Red cell transfusions were given to 13.8% (n=8) of the 58 total patients during this period. Upon discharge, 89.7% (n=52) of patients were anaemic.

### Pre-operative anaemia

As mentioned above, 29.3% of patients (n=17) were anaemic upon admission in Table 1. Of the female admissions, 21.2% (n=10) were found to be anaemic. Of the male admissions, 36.8% (n=7) were anaemic. The mean haemoglobin levels of patients who were anaemic on admission were 10.2 g/dL in females (range 9.2-11.4 g/dL) and 11 g/dL in males (range 9.1-12 g/dL) in Table 2. The average age of female patients who were anaemic on admission was 83 (range 67-93). The average age of male patients who were anaemic on admission was 83.4 years old (range 70-92).

	Total (N=58)	Male (N=16)	Female (N=42)
Pre-operative anaemia	29.3% (n=17)	36.8% (n=7)	21.2% (n=10)

Post-operative anaemia	91.4% (n=53)	93.8% (n=15)	90.5% (n=38)
Anaemia at discharge	87.9% (n=51)	87.5% (n=14)	88.1% (n=37)

**Table 1:** Frequency of anaemia on admission, post-operatively and at discharge (n=58).

### Post-operative anaemia

By day 5 post-operatively, 98.3% (n=57) of patients had their haemoglobin level measured. Anaemia was found in 91.4% (n=53) of patients in Table 1. Of the 42 female patients, 90.5% (n=38) were anaemic on day 3 post-operatively, 1 female patient did not have her haemoglobin measured post-operatively. Of the 16 male patients, 93.8% (n=15) were found to have post-operative anaemia. The average haemoglobin level among all female post-operative patients was 9.7 g/dL (range 7.5-11.4 g/dL). The average haemoglobin level among all male post-operative patients was 10.6 g/dL (range 7.6-12.7 g/dL) shown in Table 2.

	Male	Female
Mean haemoglobin level of patients who were anaemic upon admission	11 g/dL (range 9.1-12 g/dL)	10.2 g/dL (range 7.6-12.7 g/dL)
Mean haemoglobin level of patients who were anaemic post-operatively	10.6 g/dL (range 7.6-12.7 g/dL)	9.7 g/dL (range 7.5-11.4 g/dL)
Mean haemoglobin at discharge	10.8 g/dL (range 8.2-14)	10.2 g/dL (range 7.9-14 g/dL)

**Table 2:** Mean haemoglobin levels on admission, post-operatively, and at discharge (n=58).

### Anaemia investigation and treatment

Post-operatively, 51.7% of patients (n=30) had iron studies performed, 56.9% of patients (n=33) had their ferritin levels measured, and 63.8% of patients (n=37) had their folate and B12 levels measured. All three investigations were performed in 43.1% of patients (n=25) while in hospital. In total 22.4% of patients (n=13) were found to meet the criteria for iron deficiency anaemia (10 females, 3 males). 6 patients were found to have folate deficiency (3 females, 3 males). No patients were found to have a B12 deficiency shown in Table 3.

	Total (N=58)	Male (N=16)	Female (N=42)
Iron studies performed during admission	51.7% (n=30)	62.5% (n=10)	47.6% (n=20)

Ferritin level measured during admission	56.9% (n=33)	62.5% (n=10)	54.8% (n=23)
Folate and B12 measured during admission	63.8% (n=37)	75% (n=12)	59.5% (n=25)
Iron studies, ferritin, folate and B12 all performed during admission	43.1% (n=25)	50% (n=8)	40.5% (n=17)
Iron deficiency detected	22.4% (n=13)	18.8% (n=3)	23.8% (n=10)
Folate deficiency detected	10.3% (n=6)	18.8% (n=3)	7.14% (n=3)
Vitamin B12 Deficiency detected	0	0	0

**Table 3:** The investigation of anaemia during admission (n=58).

Of the 13 patients found to have iron deficiency anaemia, 15.4% (n=2) were treated with IV iron infusions and 7.7% (n=1) were discharged with a prescription for oral iron replacement. Oral iron supplementation was prescribed to a further 6 patients who did not meet the criteria for iron deficiency anaemia.

Of the 6 patients who were found to have folate deficiency, oral folate replacement was prescribed to 33.3% (n=2). A further 2 patients were prescribed oral folate replacement without demonstrating folate deficiency during this admission.

In total, 13.8% of patients (n=8) received a transfusion of at least 1 unit of red cells post-operatively. Women accounted for 75% of patients (n=6) who received a transfusion and men accounted for 25% (n=2) shown in Table 4.

Post-operative anaemia detected	Total (N=53)	Male (N=15)	Female (N=38)
Transfusion of at least 1 unit of red blood cells	15.1% (n=8)	13.3% (n=2)	15.8% (n=6)
Iron deficiency anaemia detected	Total (N=13)	Male (N=3)	Female (N=10)
Treated with IV iron	15.4% (n=2)	0	20% (n=2)

Treated with oral iron	7.7% (n=1)	0	10% (n=1)
<b>Folate deficiency detected</b>	<b>Total (N=6)</b>	<b>Male (N=3)</b>	<b>Female (N=3)</b>
Folate replaced	33.3% (n=2)	33.3% (n=1)	33.3% (n=1)
<b>Vitamin B12 deficiency detected</b>	<b>Total (N=0)</b>	<b>Male (N=0)</b>	<b>Female (N=0)</b>
Vitamin B12 replaced	0	0	0

**Table 4:** Treatment of anaemia (N=53).

### Anaemia at discharge

Upon discharge, 87.9% of patients (n=51) remained anaemic. Of the 42 female patients 88.1% (n=37) were anaemic upon discharge. One female patient did not have her haemoglobin measured prior to discharge. Of the 16 male patients who had their haemoglobin measured prior to their discharge, 87.5% (n=14) were found to be anaemic.

The average haemoglobin level in female patients upon discharge was 10.2 g/dL (range 7.9-14 g/dL). The average haemoglobin level in male patients upon discharge was 10.8 g/dL (range 8.2-14).

## DISCUSSION

Anaemia is almost ubiquitous amongst hip fracture patients. We found anaemia to be present on admission in 29.3% of patients. Anaemia upon admission was notably higher amongst males with 36.8% being anaemic upon admission compared with 21.2% of females. Incidences of pre-operative anaemia in this cohort have been reported to range between 30%-45% [9].

Additionally, male sex has been found to be a risk factor for pre-operative anaemia [20]. A 2019 study from Queensland found that 45% of hip fracture patients aged over 60, were anaemic upon admission [20]. This study found a significant association between pre-operative haemoglobin levels and mortality. Similarly, a 20-year observational study conducted in Vienna, found that anaemia at admission was associated with an increase in three-month mortality. Patients with mild anaemia upon admission had a 1.5-fold increase in mortality, those with moderate anaemia a 2.6-fold increase, and those with severe anaemia a 3.6-fold increase compared to patients admitted without anaemia [21]. A 2011 study from Edinburgh emphasized that hip-fracture patients often suffer a large drop in haemoglobin caused by the trauma of their initial fracture rather than the operation itself [22]. This study recommended expedient fracture to theatre times as well as thorough pre-operative optimization.

There are also several studies which associate post-operative anaemia in hip fracture patients with several adverse outcomes. We found that 91.4% of patients were anaemic post-operatively.

Again, post-operative anaemia was slightly more prevalent amongst male patients (93.8% vs. 90.5%). A study from the Netherlands found that anaemia was present in 86% of post-operative patients, and that lower post-operative haemoglobin levels were associated with increased length of hospital stay [10]. Similarly, a Danish study found an association between low haemoglobin levels and decreased functional mobility in hip fracture patients [7]. Interestingly, a Spanish study found an increased association between lower haemoglobin levels in hip fracture patients and an increased risk for developing nosocomial infections [23].

In terms of the management of post-operative anaemia, restrictive transfusion protocols are recommended. In our hospital, a transfusion threshold of <7 g/dL is used in the absence of co-morbidities. This likely accounts for the relatively low number of patients transfused 13.8% (n=8) during this period. Other studies using more liberal transfusion thresholds have reported transfusion rates of 41.9% [16]. Several studies have shown that there is no difference in mortality or functional status when comparing liberal versus restrictive transfusion protocols. Additionally, post-operative transfusion has been associated with increased risk for development of infection [17]. The role of oral iron supplementation post-operatively is unclear, earlier trials demonstrated a statistically significant increase in haemoglobin level at 4 weeks with oral iron supplementation [24]. However, a 2010 study found that although patients treated with oral iron had greater increases in Hb levels at 6 weeks, this was not associated with a decrease in length of hospital stay or mortality reduction [14]. Of the 13 patients found to have iron deficiency anaemia, only 1 (7.7%) was discharged with a prescription for oral iron supplementation.

Intravenous iron is the recommended iron supplementation method in the association of anaesthetists international consensus statement on post-operative anaemia [15]. A Spanish group has investigated the effects of IV iron replacement on transfusion requirement, mortality and outcome. In a 2011 randomised controlled trial, they found that for patients admitted with an intracapsular hip fracture, or with an Hb >12 g/dL, the peri-operative administration of IV iron sucrose reduced transfusion requirements and post-operative infection rates by approximately 40% [25]. A 2020 retrospective study from Ohio found that patients who received IV iron when their Hb fell below 11 g/dL had a shorter length of stay as well as a 59% reduction in the odds of readmission within 30 days from initial discharge. Of the 13 patients found to have iron deficiency anaemia during this admission, 2 (15.4%) were treated with IV iron infusions.

## CONCLUSION

There is limited evidence on the optimal management of anaemia in hip fracture patients. Our study suggests that it is an under-investigated and an under-treated complication of hip fractures. We recommend using the association of anaesthetists international consensus statement on the management of peri-operative anaemia and iron deficiency to guide investigation and management of post-operative anaemia in hip fracture patients.



## DECLARATIONS

### Funding

Not Applicable.

### Conflicts of interest

Not Applicable.

### Ethics approval

The study was commenced following approval from the clinical audit committee, approval number 2885. This department oversees all quality improvement projects in our hospital and a separate ethics committee approval is not required in our institute if a quality improvement project is approved by the clinical audit committee.

### Consent to participate

Not applicable.

### Consent for publication

Received by all relevant stakeholders.

### Availability of data and material

All original data has been submitted on a supplementary excel spreadsheet.

### Code availability

Not Applicable

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