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Prevalence and causes of preoperative anaemia in elective major surgery patients

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Study conduct: F.S.H., N.S., C.P., F.N., A.M., A.W., W.K.H., C.S.

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Prevalence and causes of preoperative anaemia in elective major surgery patients

ABSTRACT: *(Should be structured for Original Articles, as per below; no more than 250 words.)*

Background: Preoperative anaemia is associated with increased morbidity and mortality in surgical patients. Recent national patient blood management guideline recommended screening surgical patients for anaemia and in particular iron deficiency anaemia, without reference to the prevalence of anaemia or iron deficiency anaemia in this patient population.

Aims: To establish the prevalence and cause of preoperative anaemia in elective major surgery patients.

Methods: Patients attending the anaesthetic pre-admission clinics from 1 July 2013 to 30 June 2014 prior to their major elective surgery in our institution were screened for anaemia and iron deficiency by measuring full blood count, iron studies and C-reactive protein. Patients who were anaemic were either further assessed in haematology clinic or had their medical records reviewed to ascertain the cause of the anaemia.

Results: Two hundred and eight (13.9%) of 1494 patients were anaemic, with a male predominance (70.7%). Fifty seven (27.4%) of them had iron deficiency anaemia. Other common causes of anaemia include underlying malignancy (18.3%), end stage renal failure (11.5%) and other chronic diseases (7.2%). In 53 patients (25.5%), the cause was unknown. Anaemia was most commonly found in patients scheduled for gastrointestinal surgery.

Conclusion: Preoperative anaemia affects 13.9% of patients undergoing elective major surgery. The most common causes are iron deficiency and chronic diseases. The cause was unexplained in 25.5% of patients with anaemia. The prevalence of anaemia in different surgical specialties may have implications on the approach to screening, particularly in resource limited areas.

KEYWORDS: *(Five key words in order of importance for indexing purposes should be supplied below the abstract and should be taken from those recommended by the US National Library of Medicine's Medical Subject Headings (MeSH) browser list at <http://www.nlm.nih.gov/>)*

Surgical procedures, anaemia, iron deficiency anaemia, prevalence

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BACKGROUND: *(Brief statement of relevant work or clinical situation, and hypothesis, if applicable.)*

Preoperative anaemia is independently associated with increased morbidity and mortality in surgical patients.¹⁻⁴ It is also a strong predictor of increased perioperative red blood cell transfusions.⁵⁻⁶ Evidence is emerging that red blood cell transfusions may impact adversely on surgical patients, including higher mortality,⁷⁻¹¹ increased risk of infection,^{7-9,12-13} and longer hospital and intensive care unit stays.^{7-8,14-15}

Patient Blood Management guideline module 2: perioperative,¹⁶ released by National Blood Authority in Australia in 2011, recommended identifying preoperative anaemia and for surgical patients with, or at risk of, iron deficiency anaemia (IDA), to receive preoperative iron therapy. However, there was no reference to the prevalence of preoperative anaemia in surgical patients, particularly IDA.

The prevalence of preoperative anaemia reported in the literature is variable, partly related to use of different definitions and partly to the patient populations studied. Using The American College of Surgeons' National Surgical Quality Improvement Program database, Musallam et al found 30.4% of non-cardiac surgery patients were anaemic, based on haematocrit.³ Similarly, Baron et al found a prevalence of 28.7%.⁴ In other surgical populations, one study found 10.5% of major orthopaedic surgery patients to be anaemic, based on haemoglobin, with approximately one-third of the anaemia related to haematinic deficiency, iron deficiency (ID) being the most prevalent.¹⁷ This study also found a high prevalence of iron deficiency (17.7%) in non-anaemic patients. In contrast, patients with colorectal cancer have a prevalence of 38% for IDA (haemoglobin <101g/L),¹⁸ and 60% for iron deficiency.¹⁹

Following the recommendations of the guideline, our institution established a multidisciplinary care pathway to screen for preoperative anaemia in patients undergoing major elective surgery. We sought to determine the prevalence of preoperative anaemia in this cohort of patients and the causes for anaemia, with a specific focus on iron deficiency.

METHODS: *(Laboratory or other techniques used, including statistical analysis. Outcome measures clearly stated.)*

This audit was approved by the institution's human research ethics committee (Project number H2013/05052).

Preoperative haemoglobin optimisation pathway

Elective surgery patients were screened for anaemia and ID. Anaemia was defined as haemoglobin <130g/L for men, and <115g/L for women, based on the reference ranges for haemoglobin in our pathology laboratory. A patient was considered to have ID if the ferritin was <30 µg/L. Full blood examination (FBE), iron studies and C-reactive protein (CRP) were ordered during surgical pre-admission clinics. CRP was used to assist with ferritin interpretation, as ferritin is an acute phase reactant, and can be elevated in the presence of inflammation. Patients who were having elective major surgery, such as cardiothoracic surgery, colorectal surgery, major joint replacements or vascular surgery, were further assessed by the anaesthetic team in the Anaesthetic Preadmission Clinics (APACs) prior to the operation. Patients who were found to have anaemia or ID were referred to the Haematology Clinic for further investigation to determine the cause(s) for anaemia and to commence treatment as required.

Participants

Patients aged 18 years or over who attended APAC during the period 1 July 2013 to 30 June 2014 and who were for elective major surgery were included. Basic patient demographic and laboratory data (FBE, iron studies and CRP) were collected.

Cause of anaemia was determined during assessment in Haematology clinic. For those anaemic patients who did not attend Haematology Clinic, the cause of anaemia was determined by reviewing the medical history and relevant blood test results, such as previous haemoglobin and creatinine. It was not possible to ascertain the cause in every patient due to the retrospective nature of the review.

Statistical analysis

Patient characteristics were summarized and reported as mean or medians (interquartile ranges) for continuous variables and as proportions for categorical variables.

RESULTS: *(Statistically significant results and relevant negative data cited.)*

Patient Characteristics

During the study period, 1494 patients attended APAC for elective major surgery (Table 1). All patients were screened for anaemia but 45 patients did not have iron studies performed. The median ferritin was 132 µg/L (IQR 70-227). Almost half of the patients were for orthopaedic surgery (n=662, 44.3%), followed by cardiac surgery (n=268, 17.9%).

Prevalence of Anaemia

Two hundred and eight out of 1494 patients (13.9%) were anaemic (Table 2). This included 147 men (17.9% of all men) and 61 women (9.1% of all women). The anaemia was not particularly marked for the majority of the patients: the median haemoglobin for men and women was 120 g/L and 107 g/L, with the lowest haemoglobin at 76 g/L and 88g/L respectively.

Gastrointestinal surgical units (upper gastrointestinal and colorectal) had the highest proportion of patients with anaemia, although the total number of patients is relatively small (154 patients). In contrast, the orthopaedic unit had the most number of patients with anaemia, but they only accounted for a small proportion of all patients undergoing orthopaedic surgery.

IDA was present in 57/208 patients (27.4% of those who are anaemic; 3.8% of total). These patients were spread across all surgical units (Table 2), with the urology unit having the least number by percentage (1.6%), and colorectal unit having the highest proportion (12.5%). Other common causes of anaemia were end stage renal failure (ESRF, 11.5%), underlying malignancy (18.3%) and chronic disease (7.2%) (Table 4). Most patients with malignancy related anaemia were undergoing definitive surgery for that malignancy.

In 53 patients, the cause of the anaemia was not able to be determined. Most of these patients have relatively mild anaemia (median haemoglobin 122 g/L and 106g/L for men and women respectively), with only 2 patients having haemoglobin < 100 g/L.

Iron deficient but not anaemic

Eighty-five patients (5.7%) had absolute ID (ferritin <30 µg/L) without anaemia (Table 2). Again, the colorectal unit had the highest percentage, followed by orthopaedic and cardiac surgery units.

DISCUSSION:

Prevalence of anaemia in surgical patients has been variable in the literature, ranging from 5% in geriatric women with hip fractures to 75.8% in patients with advanced colorectal cancer, using various definitions of anaemia.²⁰ In our cohort of elective major surgery patients, the overall prevalence was 13.9%. More than one-third of these were due to chronic diseases, such as ESRF or malignancy. IDA accounted for 27.4%, three quarters of which were new diagnoses. In just over a quarter of patients, the cause of anaemia was unknown.

The prevalence of preoperative anaemia in elective major surgery patients appears to reflect that of the general population, as our results are similar to the World Health Organisation (WHO) estimate of 15%²¹ and findings of The Third National Health and Nutrition Examination Survey in United States, which found increasing prevalence of anaemia after the age of 50, with 11.0% of men and 10.2% of women 65 years and older being anaemic.²² Nutrient deficiency, anaemia of chronic disease and unexplained anaemia each accounted for approximately one-third of the causes.²² In contrast, a population study in Portugal found higher prevalence of anaemia (19.9%), more prevalent among women, with 54.8% of anaemia due to ID.²³ A number of other studies have reported varying prevalence of preoperative anaemia, but ID usually accounted for about one-third of the causes.^{17,22,24}

The patient population with the highest proportion of anaemia in our cohort was those scheduled to have gastrointestinal surgery, either upper or lower gastrointestinal tract. This is best explained by the reason for their surgery, which is often for malignancy. Gastrointestinal malignancy can lead to anaemia from bleeding (IDA) and/or through chronic disease/inflammation, two of the most common causes for preoperative anaemia. Eighteen out of the 40 patients with anaemia in upper gastrointestinal and colorectal surgical units have IDA.

Among the patients with IDA (n = 57), 17 patients were having surgery for the cause of the IDA – resection of underlying gastrointestinal or bladder malignancy. This included 11 patients in colorectal surgery unit, 3 patients in upper gastrointestinal surgery unit and 3 patients in urology unit.

It is not surprising that chronic diseases accounted for more than one-third of anaemia, due to an ageing population and advances in healthcare, turning previously fatal illnesses into chronic diseases. Most of

the patients who had malignancy-related anaemia were scheduled to have surgery for the underlying malignancy, which should help to improve the anaemia.

The cause of the anaemia for a sizeable number of patients could not be determined. This is partly due to limited information available in the medical records when reviewed, particularly if the patients were referred from another centre for a specific surgery (e.g. cardiac surgery), or where the anaemia was relatively mild in an otherwise asymptomatic patient (majority of these patients), a “watch-and-wait” approach was adopted and further invasive investigation, such as bone marrow biopsy, was not pursued for the time being. It is possible with further investigations, the cause of the anaemia in some of these patients can be established.

Our screening also identified a group of patients who were ID without anaemia. Together with the IDA group, they accounted for 9.5% of elective major surgery patients. Unsurprisingly, more colorectal surgery patients were ID (20.2%), as most of them were undergoing surgery for gastrointestinal malignancy, which often causes ID with or without anaemia from bleeding. Other studies have also reported high rates of ID and IDA in colorectal surgery patients.^{18-19,25-26} In our cohort, cardiac surgery, thoracic surgery and orthopaedic units also had high prevalence of ID (10.4%, 9.2% and 8.6% respectively). This may be related to the use of aspirin and other non-steroidal anti-inflammatory drugs in these groups of patient, which is a known risk factor for gastrointestinal bleeding. However, this will need to be confirmed with further study looking at the causes of iron deficiency in the elective major surgery patient population.

As the prevalence of ID and IDA are different across surgical units, this has implications for preoperative screening, especially if there is only limited resources available.

While the prevalence of anaemia in our study is comparable to those published in the literature, it may be a slight underestimation, as our haemoglobin cut-off for anaemia in women is slightly lower than that of the WHO, which defines anaemia as haemoglobin below 120g/L. However, this effect is likely to be small and not all published studies used the WHO cut-offs for anaemia.

The rate of ID in our study is based on ferritin < 30µg/L (absolute ID). This may have underestimated the true prevalence of ID since ferritin is an acute phase reactant and is raised at times of inflammation, as reflected by CRP. It is possible some of the patients with low normal ferritin (30-100µg/L) and CRP >10 mg/L may actually be iron deficient.

The standard iron study measures serum iron, serum transferrin, transferrin saturation and serum ferritin, none of which is a good marker for ID in the setting of concurrent inflammation. It has been proposed that when ferritin is >100µg/L in the setting of inflammation, true iron deficiency is unlikely,²⁷ however this requires further validation. Other tests that may help are soluble transferrin receptor and hepcidin. The former is elevated in ID and low-normal in chronic inflammation, but is not a routine test in our diagnostic laboratory, hence no results were available. Hepcidin is low in ID and high in chronic inflammation, but has mainly been used in the research setting.

Although this is a single centre study, our institution serves a catchment area of more than 1.2 million people across eight local government areas, giving some confidence that the results are likely to reflect that of the overall elective major surgery patient population.

CONCLUSION: *(Referable to the aims of the study and may include suggestions for future action.)*

The overall prevalence of preoperative anaemia in elective major surgery patients is 13.9%, similar to that of the general population, with variations between surgical units. The main reversible cause of anaemia is iron deficiency, which is most common in patients scheduled for gastrointestinal surgery. These data will assist in the design of future preoperative anaemia screening and intervention programs.

REFERENCES: (Supply a maximum of 60 references. Style and punctuation should conform to the Vancouver format. List all authors when six or fewer; when seven or more list the first six and add *et al*. The issue number should not be quoted. Website references – treat as other reference. In the text, references should be cited using superscript Arabic numerals in the order in which they appear. If cited only in tables or figure legends number them according to the first identifications of the table or figure in the text. In the reference list, the references should be numbered and listed in order of appearance in the text.)

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Table 1. Patient characteristics. Values are median (range) or number (proportion).

Male:Female	822 (55.02%) : 672 (44.98%)
Age (years)	65.2 (18-92)
Haemoglobin (g/L)	
Male	144 (76-186)
Hb <130g/L (n = 147)	120 (76-129)
Female	135 (88-171)
Hb <115g/L (n = 61)	107 (88-114)
Ferritin† (µg/L)	132 (5-3450)
†45 patients did not have ferritin levels taken	

Table 2. Prevalence of anaemia, iron deficiency anaemia and iron deficiency without anaemia by surgical units. Values are number.

Surgical unit	Number (%)* by surgical unit	Anaemia				Iron deficiency anaemia			Iron deficiency without anaemia	
		Male	Female	Number	% of surgical unit	Number	% of surgical unit	% of anaemic patients	Number	% of surgical unit
Orthopaedic	662 (44.3%)	45	23	68	10.3%	14	2.1%	20.6%	43	6.5%
Cardiac	268 (17.9%)	23	12	35	13.1%	11	4.1%	31.4%	17	6.3%
Urology	126 (8.4%)	12	2	14	11.1%	2	1.6%	14.3%	4	3.2%
Thoracic	109 (7.3%)	19	2	21	19.3%	4	3.7%	19.0%	6	5.5%
Colorectal	104 (7.0%)	16	11	27	26.0%	13	12.5%	48.1%	8	7.7%
Vascular	75 (5.0%)	13	0	13	17.3%	4	5.3%	30.8%	1	1.3%
Hepatobiliary	68 (4.6%)	6	4	10	14.7%	2	2.9%	20.0%	4	5.9%
Upper gastrointestinal	50 (3.3%)	8	5	13	26.0%	5	10.0%	38.5%	1	2.0%
Ear, Nose and Throat	23 (1.5%)	5	1	6	26.1%	2	8.7%	33.3%	1	4.3%
Breast	9 (0.9%)	-	1	1	11.1%	0	0	0	0	0
	1494	147	61	208	13.9%*	57	3.8%*	27.4%	85	5.7%*

*As a proportion (%) of the entire surgical cohort (n = 1494)

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Table 3. Causes of anaemia. Values in number (proportion).

Iron deficiency	43 (20.7%)
Treated iron deficiency	14 (6.7%)
Malignancy $\pm$ chemotherapy	38 (18.3%)
End stage renal failure	24 (11.5%)
Other chronic diseases	15 (7.2%)
Thalassaemia	8 (3.8%)
Non-malignancy related bleeding	4 (1.9%)
Blood loss from surgery within preceding 3 months	4 (1.9%)
B12 deficiency	2 (1.0%)
Recent hospitalisation for medical illness	1 (0.5%)
Folate deficiency	1 (0.5%)
Autoimmune haemolytic anaemia	1 (0.5%)
Could not be determined	53 (25.5%)
Total	208 (100%)

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