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Effect of preoperative anaemia on postoperative complications in low resource settings

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Abstract

Background—In high resource settings, even mild anaemia is associated with an increased risk of postoperative complications. Whether this is true in low resource settings is unclear. We aimed to evaluate the effect of anaemia on surgical outcomes in the Republic of Congo and Madagascar.

Method—Retrospective chart review of 2064 non-pregnant patients undergoing elective surgery with Mercy Ships. Logistic regression was used to determine the association between pre-operative anaemia and predefined surgical complications, and adjusted for age, gender, surgical specialty, and country.

Results—The average age of patients was 27.2 years; 56.7% were male. 62% of patients were not anaemic, and 22.7%, 13.9% and 1.4% met sex-related criteria for mild, moderate and severe anaemia. In adjusted analyses, the severe anaemia group had an 8.58 [3.65, 19.49] higher odds of experiencing any surgical complication ($p < 0.001$) compared to non-anaemic patients. Analysis of each complication showed a 33.13 [9.57, 110.39] higher odds of unexpected ICU admission ($p<0.001$); a 7.29 [1.98, 21.45] higher odds of surgical site infection ($p<0.001$); and 7.48 [1.79, 25.78] higher odds of requiring hospital readmission ($p<0.001$). Evaluating other anaemia categories, only those with moderate anaemia had a higher risk of requiring ICU admission (odds ratio 2.75 [1.00, 7.04], ($p = 0.04$) compared to those without anaemia.

Conclusion—Our results indicate that in low income settings, severe anaemia is associated with an increased risk of postoperative complications including unexpected ICU admission, surgical site infection, and hospital readmission, whereas mild anaemia was not associated with increased postoperative complications.

Keywords

global surgery; outcomes; patient safety

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Introduction

The World Health Organisation defines anaemia as an insufficient circulating red cell mass, with a haemoglobin concentration of < 13.0 g/dL for men and < 12.0 g/dL for women [1]; and subdivides anaemia into three categories: mild, moderate and severe [2]. In high resource settings, even mild anaemia adversely effects surgical outcome and is independently associated with increased postoperative mortality, complications, and length of hospital stay [3–6]. Therefore non-treatment of perioperative anaemia is considered 'substandard practice' [7, 8]. Whether we can apply these findings to low income countries is an important question since the aetiology of anaemia between low and high income settings differs due to differences in the prevalence of malnutrition, life-expectancy, and age-related illness [9–11]. Anaemia is disproportionately prevalent in low-socioeconomic settings where patients often cannot afford iron supplementation[10, 12, 13].

The only data on the effect of anaemia on perioperative outcomes in low income settings comes from one combined retrospective and prospective study in India [14]. Retrospective analysis of 452 patients undergoing hernia, hydrocele and hysterectomy showed anaemia was associated with increased spinal headache and fever. Prospective analysis of 214 patients showed no statistically significant correlation between anaemia and surgical outcome. The incidence of complications did not increase with the severity of anaemia in either arm.

Given the discrepancy in the literature between low and high income countries, we aimed to evaluate the effect of preoperative anaemia on surgical outcome in a larger cohort of patients in a low income setting. We report our experience of 2073 patients undergoing surgery on board the *Africa Mercy* in the Republic of Congo and Madagascar.

The *Africa Mercy* is an 82 bed, non-governmental hospital ship working in Africa providing a wide range of free elective surgeries. The hospital is staffed by mainly western volunteers, and outpatient and rehabilitation services are provided for up to 10 months post-operatively.

Materials and Methods

Study data were obtained by retrospective chart review of all non-pregnant patients undergoing elective surgical procedures on board the *Africa Mercy* between September 2013 and May 2015. Surgical specialties evaluated included: general, plastics and reconstructive, orthopaedic, maxillofacial and gynaecological/obstetric fistula surgery. All procedures were open rather than laproscopic, and were classified as clean or clean-contaminated. In maxillo-facial and obstetric fistula surgery the majority were clean-contaminated, whereas the majority of general, plastics and orthopedic procedures were clean, with only the occasional clean-contaminated procedure. Antibiotic prophylaxis is routinely administered and protocol driven; blood transfusion is not protocolised but use of a transfusion trigger of 7–8 g/dL is recommended to surgeons and anaesthesia providers. The majority of patients are fit and healthy as classified by the American Society of Anesthesiology (ASA) score or 1 or 2 and therefore have few co-morbidities. Patients with cardiopulmonary symptoms have Lee's revised cardiac index calculated [15] and patients determined as class 4 are cancelled, and

those deemed class 3 are discussed at a multi-disciplinary meeting to determine the risk/benefit of surgery.

The primary exposure of interest was anaemia presence and severity using pre-operative haemoglobin values obtained at the time the participant was listed for surgery. The presence of anaemia and its severity was defined according to the World Health Organization classification, which classifies a participant as not anaemic, or having, mild, moderate, or severe anaemia using age and gender specific criteria [1].

The primary outcome of interest was the presence of any surgical complications. *Africa Mercy* complications are recorded contemporaneously then reviewed monthly at a Hospital Review Board, which involves review of each case history by the deputy chief medical officer, chief surgeon, chief of anaesthesia, operating room manager, ward nursing supervisor. Complications are verified, classified for impact by consensus agreement using the Dondo-Clavien classification [16], and recorded in a database. Complications were defined as: unplanned return to the operating room (OR); unexpected intensive care unit (ICU) admission; surgical site infection [17]; and other. Other consisted of readmission to hospital and 12 predefined complications [18], namely myocardial infarction; stroke, renal failure, gastrointestinal bleed, deep vein thrombosis, pneumonia, sepsis, urinary catheter associated urinary tract infection, central venous catheter associated blood stream infection, coma greater than 24 hours, cardiopulmonary arrest, and death. Bleeding was not included as a stand alone complication but is included as a reason for hospital readmission, return to the OR or unexpected ICU admissions. Patients were followed up to identify complications through hospital discharge to outpatient discharge. Any patient also representing with a surgical complication during the ships' visit was included, therefore for some patients this was a 9 month period, whereas for others it was up to 25 days.

In the primary outcome analysis, logistic regression was used to determine the association between pre-operative anaemia and any surgical complications. A priori, we decided to adjust for age, gender, surgical specialty, and country in the analysis. Subjects with missing data were excluded from the analysis. All analyses were performed using R 3.3.0. Two sided p-values of <0.05 were considered significant.

Mercy Ships International Review Board approved the study.

Results

Of 2073 subjects identified, 8 were missing pre-operative haemoglobin and one was missing age and so were excluded leaving 2064 participants. The characteristics of the participants are as detailed in Table 1. Most of the participants (62.0%) were not anaemic, with 469 (22.7%), 287 (13.9%), and 28 (1.4%) meeting sex-related criteria for mild, moderate, and severe anaemia. Participants were young, with a mean age of 27.2 ± 20.0 years and no significant age differences between anaemia categories. Although 56.7% of the overall cohort were men, only 19.7% of men met criteria for anaemia. Participants undergoing maxillofacial surgery comprised 19 out of the 28 participants with severe anaemia. When

looking at complications, there were notably no deaths or complications falling in the "other" category besides hospital readmission during this study period.

Of the participants with severe anaemia, 11 (39.3 %) experienced any surgical complication, with 6 (21.4%) requiring unexpected ICU admission, 2 (7.1%) requiring an unexpected return to the operating room, 4 (14.3%) experiencing a surgical site infection, and 4 (14.3%) requiring hospital readmission.

Those in the severe anaemia category had a significantly higher risk of complications compared to those without anaemia in both univariate (Table 2) and multivariate (Table 3) analyses. In multivariate analyses, those in the severe anaemia group had an 8.58 [3.65, 19.49] higher odds of experiencing any surgical complication ($p < 0.001$) compared to those without anaemia. Looking at each component of surgical complications, the higher odds of having any surgical complication seemed to be driven by unexpected ICU admissions (odds ratio 33.13 [9.57, 110.39], $p < 0.001$), surgical site infection (7.29 [1.98, 21.45], $p <0.001$), and hospital readmission (7.48 [1.79, 25.78], $p = 0.001$). When evaluating other anaemia categories, only those with moderate anaemia had a higher risk of unexpected ICU admission (odds ratio 2.75 [1.00, 7.04], $p = 0.04$) compared to those without anaemia.

The most common reasons for readmission were (i) surgical site infection (10/54, 18.5%); (ii) bleeding or hematoma formation requiring intervention (9/54, 16.7%); wound dehiscence not associated with infection (7/54, 13.0%). The most common reasons for return to the OR were (i) bleeding or evacuation of hematoma (16/73, 21.9%); (ii) surgical site infection requiring surgical intervention (12/73, 16.4%); and an additional six plastics patients needed re-grafting and several obstetric fistula patients required returned to the OR for ureteric stents. Sixty-six percent (21/32) of unexpected ICU admissions were maxillofacial patients for management of airway oedema where the anesthetic provider initially planned to extubate the patient after surgery, but due to concerns the patient was kept intubated and admitted to ICU overnight for extubation 12–24 hours later. Other causes were 10 cases of major blood loss greater than expected; emergency respiratory difficulties after thyroid surgery; and electrolyte disturbances requiring monitoring and replacement.

For this cohort of patients, the average length of hospital stay was 3, 6, 12, 16, 18 days for general, maxilla-facial, orthopaedic, plastics and obstetric fistula surgery, respectively. We did not measure individual transfusion requirements but data from our blood bank showed that for this cohort of 2073 patients, 91 individuals received a total of 212 units of whole blood. The majority of blood, 136 units (64%) was given to 51 maxillofacial patients.

Discussion

In our study population of elective operations performed in two low-income settings, we demonstrated that severe anaemia was associated with an increased risk of post-operative complications, whereas mild anaemia was not.

Our result that severe anaemia increases the risk of surgical site infection is similar to other studies in low income countries [19–22]. However, our finding that moderate and severe anaemia also increases the risk of other postoperative complications is novel and differs

from the only other low income study on anaemia and postoperative complications [14]. Lagoo found anaemia had little effect on postoperative complications and the incidence of complications did not increase with anaemia severity [14]. The difference may be explained by our larger sample size; categorisation of anaemia severity; and broader range of surgeries in our study.

Our results suggest that mild anaemia does not predispose to complications, in contrast to studies from high income settings [3–6]. This may be related to differing anaemia aetiologies. In high income countries, anaemia increases with increasing age and is often related to the underlying surgical disease. However, in low income countries anaemia is concentrated in pre-school age children and women [11]; and has multifactorial causes involving complex interactions between nutrition, infectious diseases and other factors [9]. Globally, 80% of haemoglobinopathies occur in low income countries and are poorly treated [23] further contributing to the burden of anaemic disease. That the anaemic population in low income countries is generally younger and fitter may mean they are better able to tolerate the demands of surgery, despite anaemia, compared with their older frailer counterparts in high income countries. Therefore, our results suggest that while preoperative treatment of anaemia is important, current trends in the literature towards aggressive treatment with for example, intravenous iron therapy for even mild anaemia, should be interpreted cautiously and may not be medically justified in low income settings [24–27].

Our finding that mild anaemia is not associated with and increase in postoperative complications may be explained by additional factors which should be considered when interpreting our results and applying them to other low income contexts. The two countries in our study, the Republic of Congo and Madagascar, both have a very low prevalence of human immune-deficiency virus (HIV) infection, 2.8% and 0.5% respectively [28, 29]. We do not routinely test patients for HIV therefore we cannot comment on the incidence of HIV in our cohort, but in countries with a higher prevalence of HIV, complications rates may be increased. Appropriate and timely antibiotic prophylaxis is known to reduce the incidence of surgical site infections and is used routinely in our hospital according to protocol, but this may not be the case in other low income countries. Most of our patients were young and with few co-morbidites

Our study has some limitations. It is retrospective in nature and we lack data on duration of surgical procedure and mean blood loss associated with the surgeries. It is restricted to two countries, Madagascar and Republic of Congo, and our participants were relatively young and undergoing elective surgeries; therefore generalization to other settings should be done with caution. Nonetheless we believe our study has a number of strengths. The sample size is large and it adds to only one prior small study on the effect of anaemia on complications in global surgery. Complications were reviewed and collected in a standardized fashion. Surgery on Mercy Ships is performed in a relatively ‘high tech’ environment and is provided free of charge; this is a strength as it eliminates confounding factors such as quality of surgery, anaesthesia, or nursing skills, lack of modern drugs and equipment, or ability to pay for medical and associated costs, which can hinder comparisons between high and low income settings.

In conclusion, our results indicate that severe anaemia predisposes to postoperative complications but mild anaemia does not. Claims that preoperative mild anaemia mandates treatment should be interpreted with caution in low income settings.

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Table 1

Baseline characteristics of patients stratified by anaemia severity.

	None	Mild	Moderate	Severe
Observations	1280	469	287	28
Age, years *	29.1 ± 19.0	26.6 ± 21.5	19.7 ± 20.4	32.1 ± 18.0
Men	763 (59.6%)	259 (55.2%)	143 (49.8%)	5.0 (17.9%)
Hemoglobin, g/dL				
Men	13.8 ± 1.5	11.6 ± 0.9	9.8 ± 0.9	5.6 ± 2.0
Women	12.8 ± 0.9	11.3 ± 0.5	9.9 ± 0.9	6.2 ± 2.3
Country				
Madagascar	521 (40.7%)	172 (36.7%)	133 (46.3%)	14 (50.0%)
Congo	759 (59.3%)	297 (63.3%)	154 (53.7%)	14 (50.0%)
Surgical specialty				
General	497 (38.8%)	164 (35.0%)	104 (36.2%)	5 (17.9%)
Gynecology	85 (6.6%)	26 (5.5%)	28 (9.8%)	2 (7.1%)
Maxillofacial	452 (35.3%)	190 (40.5%)	106 (36.9%)	19 (67.9%)
Orthopedics	70 (5.5%)	28 (6.0%)	17 (5.9%)	2 (7.1%)
Plastics	176 (13.8%)	61 (13.0%)	32 (11.1%)	0 (0%)
Complications				
Any **	105 (8.2%)	46 (9.8 %)	28 (9.8 %)	11.0 (39.3 %)
ICU admission	13 (1.0%)	6 (1.3%)	7 (2.4%)	6 (21.4%)
Return to OR	41 (3.2%)	20 (4.3%)	10 (3.5%)	2 (7.1%)
Surgical Site	45 (3.5%)	19 (4.1%)	7 (2.4%)	4 (14.3%)
Infection				
Hospital	31 (2.4 %)	10 (2.1%)	9 (3.1 %)	4 (14.3%)
Readmission				

* Values are given as mean ± standard deviation; other values given as actual number (%)

** Any complication includes unexpected ICU admission, return to the OR, surgical site infection, hospital admission, myocardial infarction, stroke, renal failure, gastrointestinal bleed, deep vein thrombosis, pneumonia, sepsis, urinary catheter associated urinary tract infection, central venous catheter associated blood stream infection, coma greater than 24 hours, cardiopulmonary arrest, and death. Some patients experienced more than one complication.

Table 2

Unadjusted risk of complication based on anaemia score. Values are odds ratios [95% confidence intervals].

	Mild vs. No Anaemia	Moderate vs. No Anaemia	Severe vs. No Anaemia
Any complication	1.22 [0.84, 1.74]	1.21 [0.77, 1.85]	7.24 **** [3.21, 15.69]
ICU admission	1.26 [0.44, 3.22]	2.44 * [0.91, 6.00]	26.58 **** [8.69, 74.23]
Return to OR	1.35 [0.77, 2.29]	1.09 [0.51, 2.12]	2.32 [0.37, 8.15]
Surgical Site Infection	1.16 [0.66, 1.97]	0.69 [0.28, 1.44]	4.57 *** [1.30, 12.45]
Hospital Readmission	0.88 [0.41, 1.74]	1.30 [0.58, 2.66]	6.72 **** [1.89, 18.69]

* p<0.1;

** p<0.05;

*** p<0.01;

**** p<0.001

Table 3

Adjusted risk of complication based on anaemia score. Values are odds ratios [95% confidence intervals]. Models adjusted for age, gender, surgical specialty, country, and anaemia score based on WHO categories.

	Mild vs. No Anaemia	Moderate vs. No Anaemia	Severe vs. No Anaemia
Any complication	1.25 [0.85, 1.81]	1.16 [0.72, 1.83]	8.58**** [3.65, 19.49]
ICU admission	1.24 [0.43, 3.20]	2.75** [1.00, 7.04]	33.13**** [9.57, 110.39]
Return to OR	1.29 [0.73, 2.23]	0.97 [0.45, 1.92]	2.33 [0.36, 8.59]
Surgical Site Infection	1.22 [0.68, 2.12]	0.82 [0.33, 1.79]	7.29**** [1.98, 21.45]
Hospital Readmission	0.97 [0.43, 2.02]	0.99 [0.42, 2.14]	7.48*** [1.79, 25.78]

* p<0.1;

** p<0.05;

*** p<0.01;

**** p<0.001