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ORIGINAL ARTICLE

PREOPERATIVE ANAEMIA IN SOUTH AFRICAN NON-CARDIAC SURGERY PATIENTS

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ABSTRACT

Purpose: *Reports of preoperative anaemia from African non-cardiac surgery settings are rare. This might have implications with regard to the perioperative management of non-cardiac surgery patients in these settings. We sought to report the prevalence, associated characteristics, and impact of preoperative anaemia on major postoperative complications in South African non-cardiac surgery patients.*

Methods: *This was a retrospective analysis of data (preoperative haemoglobin and red cell morphology; preoperative clinical characteristics; and major postoperative complications) from 194 adults who underwent elective non-cardiac surgery at a tertiary South African hospital. Relevant statistical analyses were performed to determine the prevalence, associated characteristics, and impact of preoperative anaemia on major postoperative complications.*

Results: *The prevalence of preoperative anaemia was 42.3%. HIV was associated with a higher risk of preoperative anaemia (p=0.024). A non-communicable disease indication for surgery was associated with a lower risk of preoperative anaemia (p=0.009). A crude association between preoperative anaemia and increased major postoperative complications was observed (p=0.003).*

Conclusion: *Preoperative anaemia is prevalent in our surgical population. HIV and a non-communicable disease indication for surgery are associated with preoperative anaemia. The risk of major postoperative complications appears higher in patients with preoperative anaemia.*

Keywords: *Anaemia, Preoperative Period, Prevalence, Risk Factors, Postoperative Complications*

INTRODUCTION

Anaemia is a common haematological disorder, afflicting almost one-third of the global population (1). The World Health Organisation (WHO) defines anaemia as a haemoglobin (Hb) measurement of <12.0 g/dL in women and <13.0 g/dL in men (2). Up to 22% of the general South African (SA) adult population is anaemic (3). Overseas studies suggest that estimates for anaemia might be higher in patients presenting to hospital for surgical intervention than in the general population (4). Preoperative anaemia (PA) is a risk factor for poor postoperative outcomes in overseas non-cardiac surgery populations (5-7).

However, the prevalence of PA, associated characteristics, and its impact on major postoperative complications (MPC) in SA non-cardiac surgical patients is poorly described. A better understanding of these aspects of PA in a SA setting would have important implications with regard to how public health specialists design interventions and patient management strategies aimed at reducing the burden of disease attributed to PA in this setting.

The primary objective of this study was to report the prevalence, grading, and morphological characteristics of PA in SA non-cardiac surgery patients. The secondary objectives of this study, with reference to SA non-cardiac surgery patients, were to determine characteristics associated with PA, and to determine the impact of PA on MPC.

PATIENTS AND METHODS

Study design, study setting, and study sample:
This was a retrospective chart review involving a random sample of 194 adult elective non-cardiac surgery patients who attended the Inkosi Albert Luthuli Central Hospital in Durban, SA between 01 January 2016 and 31 March 2016.

Data source and data management:
The medical records of the aforementioned 194 patients were reviewed and data related to age, gender, indication for surgery, smoking, clinical comorbidity, medication use, albumin, and Hb measurements were collected using an electronic spreadsheet. The postoperative course of all patients was reviewed until hospital discharge.

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During this process, major postoperative complications, defined according the method recommended by Dindo and colleagues (8), were also noted. Preoperative hypoalbuminaemia was determined from the aforementioned albumin measurements using a threshold of <32.0 g/L (9). Preoperative anaemia was determined from preoperative Hb measurements using diagnostic thresholds recommended by the WHO (2). Anaemia was graded using WHO thresholds (severe anaemia: Hb < 8.0 g/dL in both females and males; mild-moderate anaemia: Hb 8.0-12.0 g/dL in females, and Hb 8.0-13.0 g/dL in males) (2). Conventional measurement thresholds for Mean Corpuscular Volume (MCV) were used to classify anaemia based on red cell morphology (10).

Statistics:

Descriptive statistics were used to present the characteristics of the study sample. Descriptive statistics were also used to present the prevalence, grading, and morphological characteristics of PA. The relationship between various characteristics and PA was determined through crude (Mann-Whitney test, chi-squared test, or Fishers exact test) and adjusted (logistic regression) statistical analyses. Results for the crude statistical analyses are presented as frequencies and percentages or medians with interquartile range (IQR). Characteristics attaining a p-value <0.20 in the crude statistical analysis were included in the adjusted statistical analysis to ensure a parsimonious regression model was obtained. Results for the adjusted statistical analysis are presented as odds ratios (OR) with 95% confidence intervals (95% CI). We also performed a crude statistical analysis which sought to identify any potential association between PA and MPC. A p-value <0.05 was considered statistically significant. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 24.0 (IBM Corp, USA).

Ethical approval:

This study was approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal, SA (Protocol BE248/17).

RESULTS

Description of study sample characteristics:

Characteristics of the study sample are presented in **Table 1.** The median age of the study sample was 45.5 (IQR: 33.0-61.0) years old, with just under half of patients being male (43.3%). One in every 6 patients were smokers. Non-communicable disease was the primary indication for surgery for the most of the study sample (68.6%, 133/194). Seventeen percent of patients (33/194) had an ASA score of more than 2 points. Chronic statin, aspirin, and non-steroidal anti-inflammatory drug (NSAID) use was established in 7.7% (15/194), 7.7% (15/194), and 7.2% (14/194) of the study sample. Hypertension and HIV were the two most prevalent comorbidities, afflicting 35.6% (69/194) and 23.7% (46/194) of the study sample.

Prevalence, grading, and classification of PA:

Figure 1 outlines the prevalence, grading, and classification of PA in the study sample. Approximately 42% (95% CI: 35.3-49.2%) the study sample (82/194 patients) had PA. Furthermore, four of the 82 patients with PA (4.9%) were graded as having severe anaemia, while the remaining 78 patients (95.1%) were graded as having mild-moderate anaemia. Only 75/82 anaemic patients had MCV measurements performed. Of these 75 patients, 11 (13.4%) had microcytic anaemia, 58 (70.7%) had normocytic anaemia, and seven (8.5%) had macrocytic anaemia.

Crude statistical analysis:

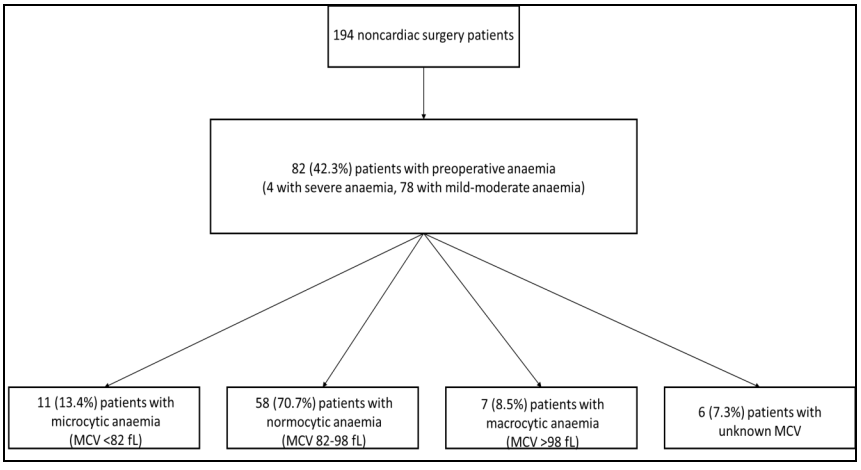
Table 2 shows results of the crude statistical analysis investigating possible associations between several characteristics and PA. Of the 19 characteristics investigated, only six were found to be crudely associated with PA. These were: increasing age (p=0.044), indication for surgery (p<0.001), smoking (p=0.030), renal failure (p=0.022), HIV (p=0.025), and hypoalbuminaemia (p=0.003). There were two characteristics with p-values which did not meet the requirement for statistical significance, but did meet the requirement for inclusion in the logistic regression analysis. These were: ASA status (p=0.082) and vascular disease (p=0.164).

Adjusted statistical analysis:

Table 3 shows the results of the adjusted statistical analysis used to identify characteristics independently associated with PA in our study sample. Eight characteristics met the criteria for inclusion in the logistic regression model. However, only two characteristics were found to be independently associated with PA. Specifically, HIV infection was found to be associated with a higher risk of presenting with PA (OR: 2.51, 95% CI: 1.13-5.56, p=0.024). Furthermore, patients with an indication for surgery related to non-communicable disease were found to be at a lower risk of presenting with PA (OR: 0.29, 95% CI: 0.11-0.73, p=0.009).

Table 1: Description of the study sample.

Characteristic	n (% of entire study sample)
Median age in years (IQR)	45.5 (33.0-61.0)
Male gender	84 (43.3)
Smoker	32 (16.5)
Indication for surgery: Infection (Abscess, tuberculosis, surgical site infection, catheter-associated infection)	33 (17.0)
Indication for surgery: Non-communicable disease (Cancer, musculoskeletal disease)	133 (68.6)
Indication for surgery: Trauma/injury (Motor vehicle accidents)	28 (14.4)
ASA score: >2 points	78 (40.2)
ASA score: ≤2 points	33 (17.0)
ASA score: Unknown	83 (42.8)
Chronic statin users	15 (7.7)
Chronic aspirin users	15 (7.7)
Chronic NSAID users	14 (7.2)
Vascular disease	5 (2.6)
Metastatic cancer	12 (6.2)
Peptic ulcer	10 (5.2)
Chronic obstructive pulmonary disease	14 (7.2)
Renal failure	14 (7.2)
Stroke	6 (3.1)
Ischaemic heart disease	12 (6.2)
Heart failure	5 (2.6)
Hypertension	69 (35.6)
Diabetes	18 (9.3)
HIV	46 (23.7)
Albumin: <32.0 g/dL	14 (7.2)
Albumin: ≥32.0 g/dL	102 (52.6)
Albumin: Unknown	78 (40.2)



PA: Preoperative anaemia, MCV: Mean corpuscular volume.

Figure 1: Prevalence, grading, and classification of PA.

Table 2: Results of the crude statistical analysis expressed as frequencies (%) or medians (IQR).

Characteristic	Patients with PA (n=82)	Patients without PA (n=112)	p-value
Median age in years (IQR)	40.0 (32.8-57.3)	49.0 (34.5-61.0)	0.044
Male gender	35 (42.7)	49 (48.3)	0.882
Smoker	8 (9.8)	24 (21.4)	0.030
Indication for surgery			<0.001
Infection	22 (26.8)	11 (9.8)	
Non-communicable	43 (52.4)	90 (80.4)	
Trauma/injury	17 (20.8)	11 (9.8)	
ASA score			0.082
≤2	26 (31.7)	52 (46.4)	
>2	18 (22.0)	15 (13.4)	
Unknown	38 (46.3)	45 (40.2)	
Chronic statin use	6 (7.3)	9 (8.0)	0.853
Chronic aspirin use	5 (6.1)	10 (8.9)	0.466
Chronic NSAID use	5 (6.1)	9 (8.0)	0.606
Vascular disease	4 (4.9)	1 (0.9)	0.164
Metastatic cancer	3 (3.7)	9 (8.0)	0.211
Peptic ulcer	4 (4.9)	6 (5.4)	0.999
Chronic obstructive pulmonary disease	5 (6.1)	9 (8.0)	0.606
Renal failure	10 (12.2)	4 (3.6)	0.022
Stroke	3 (3.7)	3 (2.7)	0.699
Ischaemic heart disease	4 (4.9)	8 (7.1)	0.518
Heart failure	2 (2.4)	3 (2.7)	0.999
Hypertension	27 (32.9)	42 (37.5)	0.511
Diabetes	8 (9.8)	10 (8.9)	0.844
HIV	26 (31.7)	20 (17.9)	0.025
Albumin			0.003
<32.0 g/dL	12 (14.6)	2 (1.8)	
≥32.0 g/dL	41 (50.0)	61 (54.5)	
Unknown	29 (35.4)	49 (57.7)	

Table 3: Results of the adjusted statistical analysis.

Characteristic	Sub-category	OR (95% CI)	p-value
Age (per year increase)	N/A	1.00 (0.98-1.02)	0.963
Smoker	Yes	0.55 (0.21-1.42)	0.216
	No	Reference	-
Indication for surgery	Non-communicable disease	0.29 (0.11-0.73)	0.009
	Trauma/injury	1.10 (0.33-3.62)	0.879
	Infection	Reference	-
ASA score	>2	2.13 (0.77-5.89)	0.146
	Unknown	1.66 (0.82-3.39)	0.161
	≤2	Reference	-
Vascular disease	Yes	1.45 (0.08-27.77)	0.806
	No	Reference	-
Renal failure	Yes	2.40 (0.58-9.92)	0.226
	No	Reference	-
HIV	Yes	2.51 (1.13-5.56)	0.024
	No	Reference	-
Albumin	<32.0 g/dL	3.74 (0.61-22.95)	0.154
	Unknown	0.84 (0.42-1.68)	0.612
	≥32.0 g/dL	Reference	-

Association between PA and MPC:
A total of 12 MPC were noted in this study. These included: 3 deaths (25.0%), 8 unplanned reoperations (66.7%), and 1 unplanned admission to a critical care unit (8.3%). The proportion of patients suffering MPC was found to be higher in the anaemic group versus the non-anaemic group (10/82 patients - 12.2% versus 2/112 patients - 1.8%, p=0.003). This translated to a crude, almost 8-fold increase in risk for MPC in the anaemic group when compared with the non-anaemic group (Crude OR: 7.64, 95% CI: 1.63-35.88).

DISCUSSION

Just over 40% of our study sample had PA. This prevalence estimate is much higher than that reported for the general SA adult population (3), but is similar to the pooled prevalence estimate of non-cardiac surgery studies reported in the systematic review by Fowler and colleagues (5). Considering that the study by Fowler et al., was comprised primarily of data from developed countries (5), our findings appear to confirm the prevalence of PA might be similar between developed- and developing-world settings.

Most patients with PA in our study sample were diagnosed with mild-moderate anaemia. This is similar to findings from a study by Musallam et al., wherein milder forms of PA were predominant (7). Normocytic anaemia was common in study sample. Anaemia of chronic disease is the most frequently encountered normocytic anaemia, and the second most common form of anaemia worldwide (11). This form of anaemia is often associated with, amongst other conditions, chronic infectious disease (11). Considering the chronic infectious disease burden SA is currently facing (12), our findings related to normocytic anaemia are to be expected.

We found patients with HIV had a 2.5-fold higher risk of presenting with PA when compared with HIV -uninfected patients. South Africa is amongst the countries most severely impacted by HIV, with the population prevalence of HIV estimated at 10% (2). Anaemia is a common clinical feature in patients with HIV, and can result from a number of mechanisms which decrease red cell production, increase red cell destruction, or promote ineffective red cell production (13). Furthermore, the published literature suggests that anaemia is associated with reduced survival in HIV-infected patients (14). Of note, antiretroviral therapy initiation in patients with HIV infection is associated with a reduction in the occurrence of anaemia (15).

It is therefore important that 1) Surgical patients are screened for HIV infection, and 2) Surgical patients with HIV infection are provided access to antiretroviral therapy.

We also found that a non-communicable disease indication for surgery was associated with a 71% reduction in risk for PA when compared with patients who had an infectious indication for surgery. While clinical studies comparing rates of PA amongst patient groups with different indications for surgery are lacking, evidence from nonsurgical settings suggest that a large proportion of anaemia in southern Sub-Saharan Africa can be attributed to infectious disease (1). This might explain our findings for a higher risk of PA in patients where the indication for surgery was infection. Patients with sepsis or infection should be carefully evaluated for Hb correction prior to their surgical procedures.

We found that patients with PA were at an almost 8-fold higher risk of developing MPC when compared with patients who did not have PA. A systematic review by Fowler and colleagues (5), found an almost 3-fold increase in risk of postoperative mortality in non-cardiac surgery patients with PA (OR: 2.87, 95% CI: 2.10-3.93, p<0.001). Applying two adjusted statistical models to non-cardiac surgery patient data, Musallam et al., found PA to be associated with a higher risk of cardiac complications (45-77%), respiratory complications (33-77%), neurological complications (5-16%), wound complications (12-56%), sepsis (24-83%), and venous thromboembolism (33-57%) (7). In their study of data from the EuSOS study, Baron and colleagues also reported higher postoperative mortality in patients with PA (6). Baron et al., also reported postoperative admission to intensive care to be greater in patients with PA than in those patients who had normal Hb measurements (6).

While we were only able to conduct a crude statistical analysis related to MPC, our findings are in agreement with the studies of Fowler et al.,(5) Musallam et al.,(7) and Baron et al.,(6) in that a harmful association between PA and postoperative complications was observed. Seeing that our findings have importance with regard to the identification and management of PA, we recommend that further research be done to confirm the observed association between PA and postoperative complications in developing-world settings.

There were limitations to our study. This was an analysis of data from a tertiary level healthcare facility in a developing-world country, and therefore our findings might not be generalizable.

Iron studies are not performed as standard of care at our facility, and we were unable to determine the potential impact of iron deficiency in our study population.

We only included patients undergoing elective surgical procedures in our study. Lastly, this study only reports on inpatient complications. The aforementioned limitations are required to be addressed in future research. While there were limitations to our study, we nevertheless present an interesting report of PA in a developing-world setting.

In conclusion, we found the prevalence and grading of PA in our study sample to be higher than that reported for the general SA adult population but similar to that reported in the published literature for other non-cardiac surgery populations.

Morphological assessment of red cells suggests normocytic anaemia to be the most common form of anaemia in our study sample. HIV infection was found to be independently associated with a higher risk of PA. When compared with patients who had an infectious indication for surgery, patients with a non-communicable indication for surgery were at a lower risk for presenting with PA. Preoperative anaemia was crudely associated with an almost 8-fold higher risk of developing MPC. The findings of this research might have important implications with regard to the management of PA in developing-world non-cardiac surgery patient populations. Further research is required to confirm the findings of our study.

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