ORIGINAL ARTICLE

Endoscopic findings among geriatric patients with anaemia and chronic kidney disease at a tertiary teaching hospital in Malaysia

Wan Rohaslizan Wan Daud, MMed[1], Rafiz Abdul Rani, MMed[2], Wong Zhiqin, MRCP[3], Shamsul Azhar Shah, PhD[4], Hazlina Mahadzir, MRCP[5], Raja Affendi Raja Ali, MRCP[3]

[1]Nephrology Unit, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia, [2]Gastroenterology Unit, Faculty of Medicine, Universiti Teknologi MARA, Sungai Buloh, Selangor, Malaysia, [3]Gastroenterology Unit, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia, [4]Department of Community Health, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia, [5]Geriatric Unit, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

ABSTRACT

Background: Older people with chronic kidney disease (CKD) may be anaemic due to various reasons, and they are vulnerable to various consequences. One of the most important causes of anaemia to be recognised in this population is gastrointestinal loss. The outcome can be improved by early detection, careful investigation, and suitable therapies. There is currently no standardised grading scale or reliable indicators to assist clinicians on handling gastrointestinal workup in elderly CKD patients who are anaemic.

Methods: A cross-sectional study of 171 people aged 60 and over who had CKD (stages 3–5), including those on Renal Replacement Therapy (RRT) and anaemia. Using oesophagogastroduodenoscopy, colonoscopy, and double balloon endoscopy, we analysed the endoscopic findings and calculated the prevalence of anaemia secondary to gastrointestinal disease. Haemoglobin, mean corpuscular volume (MCV), mean corpuscular haemoglobin concentration (MCHC), mean cell haemoglobin (MCH), iron panels, and immuno-faecal occult blood test (iFOBT) were evaluated to predict the diagnostic utility of each parameter in relation to gastrointestinal disorder in the elderly CKD population.

Results: Abnormal endoscopic findings were obtained by upper and lower endoscopy in 98 individuals (57.3%). Upper endoscopy revealed the most prevalent lesions to be gastritis, gastric ulcer, and duodenal ulcer. The upper and lower endoscopies revealed a total of 14.0% malignant and pre-malignant lesions. T-test and receiver-operating characteristic (ROC) curve were performed on all haematological parameters and iron panels. Low ferritin level (less than 100 ng/mL) and combination with low transferrin saturation (less than 20%) have a significant p value less than 0.05. None of these variables had a significant area under the curve (AUC) of more than 0.75.

Conclusion: Positive endoscopic findings of anaemia are common in the older population at various stages of CKD, regardless of age, gender, or race. Malignant and pre-malignant lesions are not uncommon in older CKD patients. In the older CKD population, GI inflammation and ulceration are common lesions. Serum ferritin and TSAT levels are useful indicators of GI disorder in this population. Endoscopic evaluation as part of anaemia workup in the older people with CKD should not be ruled out.

KEYWORDS:
Anaemia ,Chronic Kidney Disease, Geriatrics, Endoscopy

INTRODUCTION

Anaemia in geriatric population is associated with a very wide range of complications, including increased risk for mortality, cardiovascular disease, cognitive dysfunction, longer hospitalisation for elective procedures and comorbid conditions, reduced bone density, and falls and fractures.[1] Anaemia is a common problem encountered by physicians in this population on a daily basis. It is a global issue that affects both developed and developing countries worldwide. World Health Organization (WHO) has defined anaemia in adults as low haemoglobin level, i.e., below 13 g/dL in men and below 12 g/dL in women.[2] Anaemia in older people has been associated with a progressive decline in their functional status, predisposing to cardiovascular complications, leading to recurrent hospitalisation, cognitive impairment, and high burden of mortality among this population.[3] Based on the WHO criteria for anaemia, the prevalence of anaemia among the geriatric population aged 65 years and above has been reported in several large studies, and these varied by age group, race, gender, and their underlying medical problems.[3-6] As the age progresses, the degree of anaemia became more salient. Older individuals were noted to have a higher prevalence of anaemia.[7] There are other predisposing factors that should also be considered in anaemia in older people, including the smoking status, their residence, physiological status, and history of multiple hospital admissions.[2,4,5]

Defining the normal haemoglobin level among geriatric population is crucial in establishing the aetiology of anaemia and in monitoring the effects of treatment and its outcome.

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Corresponding Author: Hazlina Mahadzir
Email: drhazlina2013@gmail.com

Due to the increased prevalence of lower haemoglobin levels in older population, as well as increased risk of multiple co-morbidities leading to anaemia, determining the cause of anaemia can be challenging, especially in the setting of concurrent chronic kidney disease (CKD).

Anaemia in the older people with CKD is a manifestation of multi-factorial process. Deficiency of Erythropoiesis Stimulating Agent (ESA) is one of the commonest causes of anaemia in CKD, but in the older population, it is imperative that other causes of anaemia be excluded. This is especially true as the incidence of anaemia in older people with CKD is greater than that in the general geriatric population, and the rate of anaemia continues to rise with increasing age[8]. The older CKD population tends to have anaemia due to the pathophysiological changes related to CKD or to treatment-related complications. Some of the aetiological causes are easily corrected if identified early, whereas some aetiological causes are impossible to correct.

Nutritional anaemia is a common problem in older people, frequently manifesting as iron deficiency anaemia (IDA). In turn, iron deficiency anaemia occurs due to poor dietary intake and inadequate nutritional intake but both nutritional and chronic blood loss accounts for most of the IDA cases.[9] Patients with CKD demonstrate massive gastrointestinal bleeding that contributes to chronic blood loss leading to multiple complications. It is associated with high mortality rate.[10,11] However, the diagnosis of IDA can be complex, and various haematological parameters and iron panels are warranted to make a proper diagnosis. To date, there is no established scoring scheme or robust indicator to guide us as an approach for gastrointestinal workup in anaemic geriatric CKD patients.

Therefore, we evaluate the prevalence of anaemia secondary to gastrointestinal disorder in geriatric population with CKD (stages 3–5), and the associated endoscopic findings can help determine the diagnostic utility of each haematological variables in relation to gastrointestinal bleeding in the older CKD population. Later stages of CKD were chosen because these are when the kidneys have significant degree of reduced function, and stopping the progression of disease may induce a good impact on patient's life.

MATERIALS AND METHODS

This cross-sectional study was conducted in Universiti Kebangsaan Malaysia Medical Center (UKMMC) from April until December 2016. The sample size required was calculated based on specificity taken from a previous study and it came up to 350.11

$$FP + TN = \frac{z^2}{W^2} \times \frac{(SP\ (1\text{-}SP))}{0.05^2} = \frac{1.96^2 \times (0.7\ (1\text{-}0.7))}{} = 3.842 \times 84 = 322$$

$$N\ (sp) = \frac{FP + TN}{(1\text{-}P)} = 322 / 0.92 = 350$$

- Z = Z value (1.96 for 95% confidence level)
- W = accuracy = 0.05
- P = representing prevalence of anaemia attributed by CKD in elderly patients of more than 65 years (based on NHANES III)
- SP = specificity taken from a previous study.11
- TP = True positive
- FN = False negative

The purposive sampling methods recruited, however, was 171 patients, aged 60 years and above. The patients were those with established CKD including those on dialysis who had been referred from various multi-disciplinary clinics and inpatients. Patients were assessed by the gastroenterology team in UKMMC either in clinic or in inpatient settings prior to endoscopy investigations to decide on the need to undergo the procedure and the waiting time. Selected patients were also those with haemoglobin (Hb) concentration less than 12.0d/dL in women and less than 13.0g/dL in men, and they consented for endoscopic procedures . Patients with prior underlying malignancy and haematological or hepatic diseases are excluded from the study.

Patients included in the study were those with established presence of CKD (stages 3–5), who were on on regular dialysis, based on the level of kidney function (Glomerular Filtration Rate), i.e., less than 59 mL/min/1.73m^2 Endoscopic evaluation involved in this study includes oesophagogastroduodenoscopy (OGD), double balloon endoscopy (DBE), and colonoscopy. We included those with stages 3–5 CKD, who were on renal replacement therapy (RRT).

The CKD is staged according to the internationally accepted National Kidney Foundation – Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) guidelines (12). It is estimated based on the Glomerular Filtration Rate (GFR) using the Isotope Dilution Mass Spectrometry (IDMS) traceable Modification of Diet in Renal Disease (MDRD) Study Equation: $175 \times (Scr)^{-1.154} \times (Age)^{-0.203}$ x (0.742 if female) x (1.212 if black). Subjects with calculated eGFR from 30 to 59 mL/min/1.73m^2 were grouped into stage 3, eGFR between 15 to 29 mL/min/1.73m^2 into stage 4, and those with eGFR less than 15mL/min/1.73m^2 into stage 5.

The subjects were informed about the project details and provided written consent before participating in this study. The study protocol was reviewed and approved by the Research Ethics Committee of Universiti Kebangsaan Malaysia (Approval Code: FF-2016-133).

Initially, all patients completed the demographic questionnaire provided. Results of laboratory and stool assessment (iFOBT) were obtained within three months prior to the procedures. The study centre utilises immunochemical faecal occult blood testing (FIT), which had replaced the previous more cumbersome guaiac-based faecal occult blood. FIT does not require dietary restriction, and a single test is recommended. Although FIT has high sensitivity and specificity for colorectal cancer and adenomas, it has a lower sensitivity to the upper GI tract blood loss compared to the lower GI tract blood loss. This is due to the fact that blood gets reabsorbed in the small intestine, thereby potentially inducing a false negative and false sense of security when used in examination of the upper GI tract.

Blood tests include haemoglobin levels, MCV, MCHC, MCH, C-reactive protein (CRP), and iron panels – including serum iron, total iron binding capacity (TIBC), serum ferritin, and

Table I: Demographic characteristics of elderly anaemic CKD subjects

DEMOGRAPHIC DATA	n	%
Gender		
Male	97	(56.7)
Female	74	(43.3)
Race		
Malay	98	(57.3)
Chinese	57	(33.3)
Indian	12 (7.0)	
Others	4	(3.2)
CKD stages		
Stage 3	61	(35.7)
Stage 4	39	(22.8)
Stage 5	24	(14.0)
Stage 5 + dialysis	47	(27.5)
Age group (years)		
60–64	43	(25.1)
65–69	44	(25.7)
70–75	45	(26.3)
> 75	39	(22.8)

Table II: Types of anaemia in positive endoscopy

TYPE OF ANAEMIA	N (%)	TOTAL NO
Microcytic anaemia		10 (10.9)
Microcytic Hypochromic anaemia	7 (7.6)	
Microcytic Normochromic anaemia	3 (3.3)	
Normocytic anaemia		67 (72.8)
Normocytic Hypochromic anaemia	16 (17.4)	
Normocytic Normochromic anaemia	49 (53.3)	
Normocytic Hyperchromic anaemia	2 (2.2)	
Macrocytic anaemia	15 (16.3)	15 (16.3)

Table III: Characteristics of haematological and laboratory parameters between positive and negative finding groups

PARAMETER		POSITIVE ENDOSCOPY	NEGATIVE ENDOSCOPY	P VALUE
Haemoglobin level, g/dL ,	Mean, SD	7.2 ± 1.8	7.6 ± 1.5	0.428
MCV, fl	Median (IQR)	87.9 (84.6- 94.6)	86.1 (78.3-90.5)	0.191
MCHC,%	Median (IQR)	32.0 (30.9-32.9)	31.9 (30.4-33.0)	0.319
MCH, pg	Median (IQR)	28.2 (27.0-30.4)	27.8 (25.3-30.2)	0.389
Serum iron, ug/dL	Median (IQR)	8.9 (6.3-11.2)	7.75 (4.4-14.1)	0.497
TIBC	Mean, SD	37.12 ± 13.5	39.6 ± 15.3	0.460
TSAT,%,	Median (IQR)	18.4 (15.3-31.1)	18.3 (11.9-36.0)	0.218
Serum ferritin, ng/mL	Median (IQR)	419 (146-834)	315 (133-721)	0.449
TSAT				
<20%	N (%)	76 (56.7)	58 (43.3)	0.102
>20%	N (%)	16 (43.2)	21 (56.8)	
Ferritin				
< 100 ng/mL	N (%)	63 (60.0)	42 (40.0)	0.046*
>100 ng/mL	N (%)	29 (43.9)	37 (56.1)	
TSAT < 20%	N (%)	56 (60.2)	37 (39.8)	0.029*
iFOBT				
Positive	N (%)	14 (66.7)	7 (33.3)	0.082
Negative	N (%)	9 (40.9)	13 (59.1)	

Table IV: Endoscopic findings of elderly anaemic patients with CKD according to CKD staging

CKD STAGING FINDING	3 n (%)	4 n (%)	5 n (%)	5+D n (%)	TOTAL n (%)
OESOPHAGEAL LESION					
Oesophageal Ulcer	0 (0)	0 (0)	2 (1.2)	0 (0)	2 (1.2)
Oesophagitis Grade B	1 (0.6)	0 (0)	0 (0)	1 (0.6)	2 (1.2)
Oesophagitis Grade C	1 (0.6)	0 (0)	0 (0)	0 (0)	1 (0.6)
GASTRIC LESION					
Moderate Gastritis	3 (1.8)	2 (1.2)	3 (1.8)	2 (1.2)	10 (5.8)
Severe Gastritis	1 (0.6)	1 (0.6)	1 (0.6)	3 (1.8)	6 (3.5)
F1 Gastric Ulcer	2 (1.2)	0 (0)	0 (0)	1 (0.6)	3 (1.8)
F2 Gastric Ulcer	2 (1.2)	2 (1.2)	0 (0)	3 (1.8)	7 (4.1)
F3 Gastric Ulcer	8 (4.8)	6 (3.6)	4 (2.4)	8 (4.8)	24 (14.0)
Gastric Polyp					5 (2.9)
< 1 cm	0 (0)	0 (0)	1 (0.6)	0 (0)	
> 1 cm	1(0.6)	0 (0)	1 (0.6)	2 (1.2)	
Suspicious of cancer	2 (1.2)	0 (0)	0 (0)	3 (1.8)	5 (2.9)
DUODENAL LESION					
Duodenal Polyp					4 (2.4)
< 1 cm	0 (0)	0 (0)	0 (0)	1 (0.6)	
> 1 cm	1 (0.6)	0 (0)	1 (0.6)	1 (0.6)	
Moderate Duodenitis	1 (0.6)	0 (0)	0 (0)	1 (0.6)	2 (1.2)
Severe Duodenitis	0 (0)	2 (1.2)	0 (0)	0 (0)	2 (1.2)
F1 Duodenal Ulcer	1 (0.6)	0 (0)	0 (0)	1 (0.6)	2 (1.2)
F2 Duodenal Ulcer	2 (1.2)	2 (1.2)	2 (1.2)	3 (1.8)	9 (5.3)
F3 Duodenal Ulcer	2 (1.2)	1 (0.6)	1 (0.6)	4 (2.4)	8 (4.7)
Suspicious of cancer	1 (0.6)	0 (0)	0 (0)	1 (0.6)	2 (1.2)
COLONIC LESION					
Colonic Polyp					21 (34.4)
< 1 cm	6 (9.8)	3 (4.9)	2 (3.3)	4 (6.6)	
> 1 cm	4 (6.6)	0 (0)	0 (0)	3 (4.9)	
Rectal Polyps	1 (1.6)	0 (0)	0 (0)	0 (0)	1 (1.6)
Ulcer	2 (3.3)	0 (0)	0 (0)	0 (0)	2 (3.3)
Moderate Colitis	0 (0)	1 (1.6)	0 (0)	1 (1.6)	2 (3.3)
Severe Colitis	0 (0)	1 (1.6)	0 (0)	0 (0)	1 (1.6)
Cancerous	1 (1.6)	1 (1.6)	0 (0)	0 (0)	2 (3.3)

Table V: Histopathological examination (HPE) results of polyps from the endoscopic intervention

LESION	HPE RESULT
GASTRIC POLYPS (N=5)	
< 1.0 cm (n=1)	Foveolar type adenoma with low-grade dysplasia (1 case)
> 1.0 cm (n=4)	Hyperplastic polyps (2 cases) Foveolar metaplasia (1 case) Tubular adenoma with low-grade dysplasia (1 case)
DUODENAL POLYPS (N=4)	
< 1.0 cm (n=1)	Inflammatory polyp (1 case)
> 1 cm (n=3)	Hyperplastic polyp (1 case) Tubular adenoma with low-grade dysplasia (1 case) Neuroendocrine tumour (1 case)
COLONIC POLYPS (N=22)	
< 1.0 cm (n=14)	Hyperplastic polyps (5 cases) Tubular adenoma with low-grade dysplasia (7 cases) Not biopsied – size less than 0.3 cm (2 cases)
> 1.0 cm (n=8)	Hyperplastic polyp (1 case) Tubular adenoma with low-grade dysplasia (5 cases) Tubular adenoma with high-grade dysplasia (1 case) Tubulovillous adenoma with high-grade dysplasia and intramucosal carcinoma (1 case)

TSAT, i.e., the percentage of serum iron in the TIBC. In this study, oesophagitis with erosion or ulceration involving at least 5 mm or more of the mucosal surface, moderate to severe gastritis or duodenitis, gastric or duodenal ulcer, cancerous lesion, bleeding angiodysplasia, gastric polyp of more than 1.0 cm in diameter, and polyp of less than 1.0 cm that has proven histologically as pre-malignant or malignant lesion, were considered as positive endoscopic findings related to anaemia from the OGD. The following lesions were considered as positive endoscopy findings from the colonoscopy; one or more polyps of more than 1 cm or less than 1.0 cm in diameter that has proven histologically as pre-malignant or malignant lesion, colorectal cancer, colonic ulcer, and moderate to severe colitis.

The available data were then analysed using SPSS version 23.0 software package (IBM Corporation, Armonk, NY, USA). The data are expressed as the mean with standard deviation (SD) unless otherwise indicated. Differences in continuous variables were compared using a t-test, and differences in categorical variables were compared using a chi-square test. Receiver Operating Characteristic (ROC) curve was created with endoscopic findings (negative finding versus positive finding) as the dichotomous variables and haematological variables as the continuous variables. A p value of <0.05 was considered statistically significant in this study.

RESULTS

A total of 171 patients were enrolled in this study. Table I shows the demographic characteristics of the patients. All 171 patients had undergone OGD, only one had been subjected for DBE and 61 patients were proceeded with colonoscopy. Positive upper endoscopy findings were found in 85 patients (49.7%). Eighty-six patients with normal upper endoscopies were offered for lower endoscopy procedures but only 49 patients agreed. Thirty-nine patients who did not consent for lower endoscopy was due to refusal to drink three litres of bowel preparation fluid. Out of 49 patients, positive lower endoscopy findings were found in 22 patients (12.9%). Normal finding was noted from one DBE procedure. Of the total patients, 98 patients (57.3%) had GI lesions consistent with positive endoscopy findings from upper and lower endoscopy procedures.

Characteristics of patients with positive endoscopic finding were observed. Patients who were on RRT tend to have higher prevalence of positive endoscopic finding compared to those in the negative endoscopic finding group ($p = 0.036$). Age group, gender, race, and concurrent medications did not differ between the positive and negative endoscopic findings group ($p > 0.05$). Haematological parameter, iron panels, and iFOB of the positive endoscopic finding group were further evaluated (Table II). Out of 98 patients with positive endoscopic findings, 10 patients (10.9%) have microcytic anaemia, 67 patients (72.8%) have normocytic anaemia and the rest (16.3%) manifested as macrocytic anaemia (Table IV). Haematological parameters such as haemoglobin level, MCV, MCHC, MCH, serum iron, TIBC, TSAT, serum ferritin level, and iFOB were compared between the positive and negative endoscopic group. Only ferritin level less than 100 ng/mL and a combination of ferritin level less than 100 ng/ml and TSAT less than 20% showed a significant p value ($p < 0.05$), between the positive and negative endoscopic group (Table III). A positive correlation between serum ferritin level and CRP was 0.276 with significant p value of 0.038. ROC curves were plotted for all haematological variables and laboratory parameters, with endoscopic findings (positive and negative endoscopic group) as dichotomous variables to determine the sensitivity and specificity of each variable towards GI bleeding. However, none of these variables had a significant Area Under the Curve (AUC) of more than 0.75.

For OGD, gastritis, gastric ulcer, and duodenal ulcer were the most common lesions identified (Table IV). The prevalence of oesophageal, gastric, and duodenal lesions did not differ between the patients with CKD stages 3 to 5 ($p > 0.05$). Gastritis and duodenitis were found commonly in patients with CKD stages 3 and 4. However, gastric and duodenal ulcers were detected mostly in patients with CKD stage 5 who are on RRT. None of the ulcer cases were related to *Helicobacter pylori* or positive rapid urease test.

Out of 171 CKD subjects , 22 patients (12.9%) had positive colonoscopic findings related to anaemia. Colonic polyp size of less than 1 cm was the commoner lesions seen from the colonoscopy (Table IV). The prevalence of colonic lesions did not differ between subjects in all CKD stages 3 to 5 ($p = 0.503$). All colonoscopy had good Boston Bowel Preparation Scale (BPPS) score equal or more than 5. All the identified colonic polyps were removed endoscopically, and the suspicious cancerous lesions were biopsied. Samples were sent for further histopathology examination (HPE). Only two patients declined further endoscopic intervention; however, subsequent computed tomography scans were arranged for them, which showed malignant features of intraluminal lesions at duodenum and ascending colon. A total of 8.8% of malignant and pre-malignant lesions were detected from the lower endoscopy and 5.3% from the upper endoscopy based on HPE results (Table V). Two of the biopsied samples were not representing the lesions and were re-scheduled for repeat colonoscopy. The malignant pathologies include adenocarcinoma of stomach, intramucosal carcinoma (intestinal type) of stomach, mucosa-associated lymphoid tissue (MALT) lymphoma of duodenum, adenocarcinoma of ascending colon, and one HPE reported as foveolar metaplasia of the duodenum.

DISCUSSION

Based on Malaysian Demographic Profiles 2020, the country's ethnic groups are Bumiputera (69.4%), Chinese (23.2%) and Indian (6.7%) and others (0.7%)[13] Out of these, 6.8% of the population comprised of elderly with the age of 65 years and over.[13] Our study population represented a pattern of racial distribution almost similar to Kuala Lumpur population.

We conducted a prospective study to analyse the gastrointestinal pathological characteristic in elderly patients with CKD and to determine the prevalence of anaemia secondary to GI disorder in elderly with different stages of CKD. Anaemia in elderly population is not purely a

consequence of aging and should not be regarded as such. Apart from Erythropoietin Stimulating Agent (ESA) deficiency as a classical cause of anaemia in CKD population, other confounding causes should be evaluated especially in the elderly.[14] A thorough clinical evaluation and laboratory investigations are warranted to establish the aetiology of anaemia in elderly with CKD.

The incidence of anaemia secondary to GI disorder in adults with CKD has been reported in many previous studies. It has been found to be present in 20–75% of the population.[15-18] Hwang et al. reported that 52.9% of adult CKD patients in China were found to have bleeding-related GI lesion detected on endoscopy procedure. This finding was almost similar to our findings (57.3%); however, our study population primarily included elderly age group of more than 60 years, and did not consider the type of anaemia, whether iron deficiency anaemia or the associated erythropoietin stimulating agent (ESA) deficiency. Furthermore, it is alarming that 14% of the study participants showed either benign or malignant lesions.

From this study, we had found that those who are on RRT had a significant higher risk of GI disorder related to anaemia regardless of age, gender, and race ($p = 0.036$). Similar pattern had been observed previously by Jiing-Chyuan and colleagues.[19] They compared the incidence of GI bleeding between haemodialysis, control group, and CKD population and found higher incidence of ulcer bleeding among patients receiving haemodialysis compared to those with CKD or the control group ($p < 0.05$). This has been supported by another study from Japan by Sugimoto et al.[20] They conducted a cross-sectional study looking at the incidence of gastroduodenal ulcer in patients who are undergoing haemodialysis and healthy population. Higher rates of gastroduodenal ulcer were reported in the haemodialysis group compared to the normal population (17.8% versus 7.4%).[20] However, our study did not further classify those who are on haemodialysis or peritoneal dialysis. A plausible explanation to this finding is the use of anticoagulant during haemodialysis, commonly heparin, impaired healing ulcers due to intermittent hemodynamic instability of gastrointestinal tract during dialysis and worsening of the condition with concurrent existing ulcer that is commonly observed in those with advanced CKD with multiple co-morbidities. In general, anaemia in elderly CKD is commonly observed in female aged 65 years and above especially in African Americans with advancing CKD; however, our study has failed to demonstrate that age group, gender, and race have a significant relationship in determining anaemia-related GI lesion in elderly CKD population ($p > 0.05$).[20-23]

We also evaluated the haematological parameters, iron indices, and iFOBT to predict GI disorder consistent with anaemia. Iron deficiency anaemia (IDA) is closely related to GI blood loss. The classical markers in assessing IDA are percentage of TSAT, representing the transferrin availability for iron binding and ferritin level as a marker for iron store. In our study, we demonstrated that those patients with absolute IDA (serum ferritin less than 100 ng/ml and TSAT less than 20%) ($p=0.029$) and serum ferritin level less than 100ng/ml ($p=0.046$) have significant positive endoscopic findings from the upper and lower endoscopy. Thus, these markers are useful predictors for positive endoscopic lesion relation to anaemia in elderly patients with CKD. The pro-inflammatory marker CRP indirectly increases the synthesis of ferritin. Elevated serum ferritin level neither ruled out iron deficiency anaemia nor indicated elevated of replenished iron storage in CKD population as serum ferritin level also elevated in chronic active inflammation or infection. Persistent and low-grade inflammation has been recognised as an important component in CKD that may also lead to anaemia.[24] However low level of serum ferritin level is highly distinctive for IDA in CKD population.

Anaemia due to GI loss is often manifested as microcytosis, hypochromia, and increased erythropoiesis. Therefore, the values for MCV, MCHC, and MCH are expected to be low. However, these variables failed to predict the possibilities of positive endoscopic findings in our study. Majority of our study population manifested as normocytic normochromic anaemia rather than classical microcytic hypochromic anaemia. This might be explained by multiple confounding factors in CKD population including chronic inflammation and erythropoietin deficiency that could limit the appropriate red cell changes in this population. Hence, we suggest that in any changes of haematological indices, high, normal, or low value will not be able to rule out other causes of anaemia as per normal healthy elderly population. However, none of these variables showed a significant sensitivity or specificity in determining the incidence of anaemia related GI disorder in elderly CKD population.

Many studies have been conducted on several gastrointestinal lesions occurring in CKD population including End-Stage Renal Failure (ESRF) on RRT. In our study, we focused more on elderly patients aged 60 years and over with anaemia and CKD. To our knowledge, there has not been any other publications regarding this subject. We observed that the prevalence of each lesion is higher compared to adult CKD population. The prevalence of oesophagitis was 11.4% from our study and more commonly seen in those on RRT, slightly higher compared to other previous studies by Prakash et al., Sotoudehmanesh et al., and Hwang et al., 8.8%, 5.9%, and 1.9%, respectively, which looked at the adult population with CKD.[16,23,25] Gastritis and duodenitis occur frequently in adult CKD population especially those with advancing CKD and on RRT. Hwang et al. reported that about 17.3% of the patients were found to have erosive gastritis, 7.7% had haemorrhagic gastritis with 1.9% of erosive duodenitis and haemorrhagic duodenitis from their study population.[16] In our study, the prevalence of gastritis was about 23. 9% and duodenitis in 7.7% of patients. However, it will be premature to comment on this finding as our observation was based on macroscopic evaluation rather than histological analysis. Higher prevalence has been reported by Gheissari studied in ESRF population with the incidence of gastritis in 31% and haemorrhagic duodenitis in 20% of patients.[26] However, in our study we found that the incidence of gastritis and duodenitis was higher in CKD stages 3 and 4. Early initiation of protective agent such as Proton Pump Inhibitors (PPI) and histamine-2 receptor antagonist (H2RA) in elderly age group could explain why the incidence of GI inflammations was lesser in advanced CKD group in our study.

From our data, it was demonstrated that the prevalence of gastric and duodenal ulcers was significant, in 19.9% and 11.2%, respectively. Another study of the adult CKD population also shown a similar prevalence of duodenal ulcer in 7.7% to 11.0%.[16,23,27] The possibility of chronic uraemia renders the gastric mucosal more susceptible to acid injury due to reduction in mucosal prostaglandin content, and impaired mucosal resistance to acid injury could explain that CKD patient to be more prone to have gastric ulcer.[28] However, the exact pathophysiology of the mucosal lesion in this population is still unclear. A higher incidence of acid hypersecretion due to physiological stress of chronic illnesses and haemodialysis, concurrent use of ulcerogenic medications such as Non-Steroidal Anti-Inflammatory Agents (NSAIDS), and anticoagulant or antiplatelet for multiple co-morbidities are other contributing factors that might explain the higher incidence of gastric ulcer in the elderly CKD population.

From our data, 5.3% of the gastric lesion from upper endoscopy revealed a malignant and pre-malignant state of GI disorder.

Our study also investigated the lower GI lesion that was related to anaemia. The incidence of lower GI bleeding (LGIB) increases with age and is associated with age-specific related lesions such as malignancy.[29] In general, lower GI contribute about 85% of GI bleeding in elderly compared to 10% in upper GI and 5% in small intestine.[30] There is still a lack of specific data regarding the distribution of lower GI bleeding by location in adult CKD patients. Compared to Western Europe, the commonest causes of LGIB in Asian are haemorrhoid, fissure, and malignant colorectal neoplasms followed by benign colorectal neoplasm, ulcerative colitis, infectious colitis, ischaemic colitis, and radiation colitis.29 Similar to our study, we found colonic polyps in 37.7% of our study population, and colonic polyp size less than 1 centimetre was the commonest lesion detected from the colonoscopy (26.2%). Out of these numbers, 24.6% are proven histologically as malignant and pre-malignant state of lower GI lesions. These findings strongly support the recommendation that colonoscopy should be performed routinely in elderly aged more than 60 years with anaemia with CKD. From our data, the colonic lesions did not differ between various stages of CKD ($p > 0.005$).

Our results allow us to suggest the potential utility of upper and complete lower GI endoscopy, even in selected patients older than 85 years.

LIMITATIONS

First, we did not make it to the sample size calculated in view of time constraint. Second, limited information regarding the over-the-counter medication and protective factors for peptic ulcer disease, such as the use of Proton Pump Inhibitor (PPI) and histamine-2 receptor antagonist may limit the observation and inference from this study. Third, the practical utility of the indices studied was limited as we did not measure the erythropoietin level prior to this study. Fourth, we do not have a control group to compare our data with. Fifth, the practical utility of the indices studied was limited because we include patients who were treated with iron or erythropoiesis-stimulating agents in our study. Sixth, in view of selected anaemic cohort of CKD, geriatric patients were selected; therefore, the observed results may not totally represent the whole geriatric patients with CKD. Seventh, the sample size of the study was relatively small. Eight, the inability to perform colonoscopies or lower gastrointestinal endoscopies on all patients may not represent overall lower gastrointestinal tract abnormal findings.

RECOMMENDATIONS

Exploring the history of GI symptoms pertaining to bleeding, other co-morbidities, and the concurrent use of ulcerogenic and blood thinning medications might be a useful additional predictor for anaemia-related GI lesion in elderly patients with CKD. Initial evaluation of anaemia in elderly CKD patients should include a review of complete full blood count and iron panels. A normal MCV should not completely rule out either high or low MCV causes of anaemia. Concomitant absolute IDA must always be evaluated in the face of CKD and workup thoroughly if present. Endoscopy procedures should be performed routinely in elderly with anaemia in the setting of CKD for early detection of colorectal carcinoma and to offer early intervention as required. Our results allow us to suggest the potential utility of upper and complete lower GI endoscopy, even in selected patients older than 85 years.

CONCLUSION

The positive endoscopic findings related to anaemia are highly prevalent in elderly in various stages of CKD regardless of age group, gender, and race. The malignant and pre-malignant lesions are not uncommon amongst elderly patients with CKD. The GI inflammation and ulceration are frequent lesion observed in the elderly CKD population. Serum ferritin level and TSAT are useful indicators in determining anaemia-related GI disorder in this population. Endoscopic evaluation should not be excluded as it is an integral part of anaemia workup in elderly with CKD.

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