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Population with Large Hiatal Hernia: A Retrospective Analysis on Prevalence of Cameron Ulcers and Iron Deficiency Anaemia

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Abstract

Background and Aim: Hiatal hernia (HH) is reported to occur more commonly than previously thought with increase in number of endoscopies. Association of hiatal hernia with iron deficiency anaemia (IDA) is long reported, however there is inadequate literature on the actual factors contributing to the anaemia, including the role of Cameron ulcers and esophagitis. Our aim was to analyse the prevalence of Cameron ulcers in large HH and various factors that could attribute to anaemia in large HH.

Methods: We retrospectively analysed 117 patients (inpatient population) with large hiatal hernia (axial size ≥ 4 cm) between Jan 2008 to Sept 2015 at Monmouth Medical Centre, after excluding those with other chronic causes of anaemia. Various factors were analysed including the prevalence of Cameron ulcers, overall prevalence of anaemia, and other demographic and endoscopic details. All statistical analyses were performed using the survey commands in STATA MP 11.0.

Results: A total of 117 patients were included in the final analysis. The mean patient age was 71.1 years with a female predominance (65%). The mean size of the HH was 5.71 cm. In about 50% of the population the indication for endoscopy was Gastrointestinal (GI) bleed or anaemia or both. About 65% of the population was found to have iron deficiency anaemia. Overall prevalence of Cameron ulcers in our population was 8.5%, which increased to 17.5% with those HH ≥ 6 cm which was statistically significant (p=0.04). Esophagitis was found in 28.2% of the population. The prevalence of anaemia (<12 g/dl) in those with esophagitis was marginally higher than those without esophagitis in our study at 53.1% (17/32) and 52% (39/75) respectively, after adjusting for the presence of Cameron ulcers which was not statistically significant. There was no significant association between the use of NSAIDS/*H pylori* and the prevalence of Cameron ulcers in both univariate and multivariate analysis.

Conclusion: Large HH (size ≥ 4 cm) has a strong association with iron deficiency anaemia in more than 50% of the population. Cameron ulcers are found only in a minority of population (<10%), with increasing prevalence with increase in size of HH. NSAIDS/*H pylori* don't appear to influence the prevalence of Cameron ulcers in HH. Esophagitis appears to have a role in contribution to chronic blood loss anaemia, even though there was no statistical significance in our study. Future large prospective studies could provide additional insight into this.

Keywords: Hiatal hernia; Cameron ulcer; Esophagitis

Abbreviations: HH: Hiatal hernia; *H pylori*: *Helicobacter Pylori*; GI: Gastrointestinal

Introduction

Hiatal hernia is increasingly identified with more number of endoscopies performed, and an incidence of up to 50% during routine upper endoscopies has been documented in a study [1]. Cameron ulcers are linear gastric erosions that occur in large diaphragmatic hernia [2]. The prevalence of Cameron ulcers has been reported to be 10% to 20% in large hiatal hernias [3]. Cameron ulcers are associated with chronic blood loss anaemia although reports of severe acute life threatening bleeding exist [4]. Due to the rarity of these lesions and paucity of literature, there is no clear data on the causality of these ulcers and their association with anaemia, and other confounding factors such as concomitant NSAID use/ *H. pylori* association/ reflux esophagitis which could contribute to anaemia in patients with Hiatal hernia with or without Cameron ulcers. We try to address these issues here.

Methods and Study Population

We identified consecutive adult patients aged 18 and above from our electronic medical records at Monmouth Medical Centre, retrospectively between January 2008 to September 2015, using the ICD-9 code for hiatal hernia. Our study protocol was approved by the Institutional Review Board at Monmouth Medical Centre. Our screening included only the inpatient population. Our electronic Endoscopy procedure notes were carefully reviewed to acquire accurate and thorough information relevant for the study. Electronic records were meticulously analysed for multilevel screening for our exclusion criteria as mentioned below. For patients with multiple endoscopic procedures, the index procedure was used for data interpretation. Demographic, clinical and endoscopic details were analysed for all the patients included in our final study population.

Inclusion Criteria

Non pregnant patients above 18 years of age were included. Only those subjects with Hiatal Hernia sized ≥ 4 cm (axial size) were included in the final data interpretation. This was in accordance with the extensive review of literature available so far, indicating that very small hiatal hernia (size <3 cm) are usually clinically inconsequential.

Exclusion Criteria

Patients with Chronic Kidney Disease, Malignancies of any type, history or endoscopic documentation of peptic ulcers (other than Cameron ulcers), Colonoscopic evidence of lower gastrointestinal bleed and females with pathological gynaecological bleeding were excluded to avoid confounding factors for anaemia.

Those subjects with inadequate documentation of the Endoscopy details required for our study were also eliminated from the study. A total of 1367 patients were identified to have hiatal hernia in the initial screening based on the ICD-9. Of this, additional ICD 9 codes for chronic kidney disease (irrespective of stage) and peptic ulcerations were applied and those were eliminated from the study. In the next level of screening, the axial size of hiatal hernia was noted for all the patients from the endoscopic medical records. Those with HH size ≤ 3 cm were eliminated from the study.

If patients had colonoscopy during the same admission and were found to have an alternative cause of gastrointestinal bleed, they were also eliminated from the study. In the final screening, charts were reviewed for any history of malignancy (irrespective of stage/ resolution) and for the female population, charts were reviewed for any evidence of gynaecological bleed within the past 6 months from the endoscopic procedure. Those with positive history for the above were eliminated from the study. Any subject who escaped our multilevel screening, however found to have any of the elimination criteria during the final data collection were also eliminated from the study. Our final study population included 117 patients.

Definitions

Size of HH

We defined the size of HH by the axial length as documented in our endoscopic database. We defined large HH as those ≥ 4 cm based on the review of literature.

Anaemia

As majority of our population was female, we defined anaemia by WHO criteria for females as <12 g/dl. Haemoglobin levels on day one of admission were taken as the baseline levels to avoid confounding by intravenous fluids or other interventions including blood transfusion.

Gastrointestinal bleed (GI bleed)

GI bleed was defined as to include both occult (Positive stool guaiac) and overt gastrointestinal bleed evidenced by hematemesis or melena. Subjects with iron deficiency anaemia alone were not considered to have GI bleed.

Statistical Analysis

All statistical analyses were performed using the survey commands in STATA MP 11.0 (STATA corp, College Station, TX). Descriptive statistics were computed for all factors. These include medians, 25th and 75th percentiles, range or mean and standard deviation for quantitative variables, and frequencies and percentages for categorical factors. Continuous data are summarized as mean and standard deviation (SD).

Categorical data are summarized as frequency and group percentage. Patient characteristics were described by use of mean and range for continuous variables and proportions for categorical variables. Analysis of differences in outcomes was performed by using the Wilcoxon test for continuous variables and Chi square tests or the Fisher exact test, as appropriate, for categorical variables. P values of <0.05 were considered statistically significant.

Results

A total of 1367 patients were identified to have hiatal hernia in the initial screening based on the ICD-9. After applying our elimination criteria, our final population included 117 patients. All these patients had hiatal hernia sized 4 cm or above. Our population was female predominant with 65% females and 35% males. 76% (89/117) of our population was white with mean age of 71.1 years. Rest of the demographics are as detailed in Table 1.

We acquired data on demographics and clinical parameters including Haemoglobin, MCV, Ferritin (if details available), current use of NSAIDS/Anticoagulants and indication for endoscopy. Endoscopic details of size of HH, presence of gastritis/esophagitis/ Barrett's, *Helicobacter pylori* positivity (biopsy or stool), presence of Cameron ulcers, evidence of active bleed and any kind of endoscopic intervention done. In our population of large HH, the average Hg was 10.7 g/dl (standard deviation 2.70 and range 5-16.1).

About 55.5% (65/117) of the population were found to be anaemic (WHO criteria of <12 g/dl). Mean MCV and ferritin in our population was 86.5 and 180.5 respectively (for those data available). The average size of HH was 5.71 cm (Range 4 cm to 12 cm). The common indications for the procedure in our study were evaluation of iron deficiency anaemia 32/117 (27.3%) and gastrointestinal bleed 28/117 (24%). Rest of the indications included nonspecific complaints including intractable nausea or vomiting, dysphagia and abdominal pain/discomfort.

Cameron ulcers

Overall prevalence of Cameron ulcers in our population was 8.5% (10/117). The indications for endoscopy in our Cameron ulcer subjects were gastrointestinal bleed (50%) and iron deficiency anaemia (50%). The average size of HH in those who were positive for Cameron ulcerations was 7.44 cm (range 5 cm to 10 cm). None of these patients was positive for *Helicobacter Pylori* either by biopsy or stool antigen test. Only one of the patients had Barrett's oesophagus.

The mean haemoglobin in those with Cameron ulcers was 10.6 g/dl which was similar to our study population, as was the mean MCV of 84.65. All patients were anemic (hg<12g/dl). None of the Cameron lesions in our study were showing stigmata of high risk for re bleeding. Only two were oozing blood requiring washing. None of these lesions required endoscopic interventions. Most of them were described as linear shallow ulcerations. Three of our patients were using NSAIDs prior to the presentation. However there was no significant association between the use of NSAIDs and the prevalence of Cameron ulcers in our study in both univariate and multivariate analysis.

Variables		
Patients		N=117 Patients
Age at endoscopy (mean years)		71.1
Sex	Male	41(35%)
	Female	76(65%)
Race	White	89(76%)
	Afro American	13(11.1%)
	Hispanic	5(4.2%)
	Asian	10(8.5%)
BMI(average kg/m^2)		28.32
Average		10.7g/dl
Haemoglobin	<12	76 (64.9%)
	10 to 12	32
	<10	44
Indication for Endoscopy	GI bleed	28(23.9%)
	Evaluation of anaemia	32(27.3%)
	Others (nonspecific complaints)	57(48.7%)
Endoscopic details	Hiatal Hernia Size(mean cm)	5.71
Esophagitis	Yes	33(28.2%)
	No	84(71.8%)
Barrett's esophagus	Yes	15(12.8%)
	No	102(87.1%)
Cameron Ulcers	Total N=10 (8.5%)	
Average size of HH (cm)		7.44
No of *H Pylori* positivity		0
Hemoglobin Average(g/dl)		10.6
Hg <12		10
Hg 10-12		6
Hg <10		4

Table 1: Baseline demographic and clinical characteristics of patients.

Size of HH and prevalence of Cameron ulcers and severity of anaemia

In univariate analysis, we compared the prevalence of Cameron ulcers between those with HH >6 cm and <6 cm. We found that the prevalence was significantly higher (p=0.04) at 17.5% (7/47) in HH ≥ 6cm when compared to those with HH <6cm, for which the prevalence was 4.3% (3/70). Also we found that the degree of anaemia was significantly higher in those with larger HH (>6 cm). The mean haemoglobin for HH <6 cm was 11.3 as against HH >6 cm, which was 9.78. In univariate analysis, we analysed the degree of anaemia (hg<10 *vs.* >10) for those sizes of HH (<6 *vs.* >6 cm), which was statistically significant at P=0.007.

We also analysed all the factors that could have an independent association with Cameron ulcers using multivariate logistic regression. Only the size of HH was significantly associated with the Cameron ulcers (p=0.003). The rest of the factors including age, gender, BMI, NSAID/Anticoagulant use, esophagitis/gastritis, gastrointestinal bleed (occult and overt) did not have any influence on the Cameron ulcers in our population.

Cameron Ulcers and Esophagitis

Of the total of 117 patients in our study, esophagitis was documented in 33(28.2%) patients. Barrett's oesophagus was found in 15 (12.8%) patients, with only one patient having high grade dysplasia. Of those patients with esophagitis, 53.1% (17/32) were found to be anaemic (Hg<12 g/dl). Of those 75 patients who were negative for esophagitis in our study population, 39 (52%) were found be anaemic, with no statistical significance in the prevalence of anaemia between the two groups.

Discussion

Pathogenesis of Cameron ulcers is not clearly understood; they are thought to occur secondary to mechanical trauma at the neck of the HH secondary to diaphragmatic movement during respiration [2]. Other hypothesized factors include mucosal ischemia/mucosal injury from acid reflux/NSAID use [1,5,6]. From our study, we found that large hiatal hernias are significantly associated with Cameron ulcer in the multivariate analysis; other factors such as NSAID/anticoagulant use/*H. Pylori* were not associated with the presence of these ulcers. Although GI bleed (24 %) and iron deficiency anaemia (27.3%) were major indications for endoscopy in our study, there was no significant association between the presence of Cameron ulcers and GI bleed or iron deficiency anaemia. The prevalence of iron deficiency anaemia was 55.5 % in our entire population of hiatal hernia. Also with a prevalence of only 8.5% in our study population, Cameron ulcers could not account for the magnitude of anaemia observed in our study; other causes for iron deficiency anaemia should be considered in those with Hiatal hernia. Most of these lesions are managed conservatively with proton pump inhibitors, though a few reports of massive upper GI bleed to Cameron ulcerations requiring endoscopic intervention have been described [1,4,7,8]. In our study none of the patients with Cameron ulcers showed any stigmata for high risk GI bleed and none required endoscopic intervention. This is consistent with chronic iron deficiency anaemia that is associated with these lesions except in rare cases where they are associated with massive GI bleed as mentioned above. We also found that the prevalence of Cameron ulcers increases with size of HH. Our overall prevalence of 8.5% significantly increased to 17.5% for those with HH size ≥ 6 cm, which is similar to an observation by Gray et al. [5]. Association between iron deficiency anaemia and Hiatal hernia has been described in literature [9,10]. In our study, more than 50% of the population with hiatal hernia were found to be anaemic (Hg <12), and with our strict exclusion criteria for other causes of anaemia, they are more likely to be iron deficient unless proven otherwise. Cameron ulcers are not the only explanation for chronic blood loss in those patients with large hiatal hernia, as the prevalence of these ulcers in hiatal hernia in our study was meagre.

This finding is similar to a prospective study by Panzuto et al., where only about one third of the patients with large hiatal hernia had evidence of Cameron ulcers [11]. Another interesting factor is the common association between esophagitis (from reflux) and hiatal hernia. Whether this reflux esophagitis contributes to chronic blood loss in patients with hiatal hernia is a valid question. Ruhl et al. [9] in a prospective analysis tried to answer the above question, in which they compared the hospitalization rates of iron deficiency anaemia for those with a diagnosis of hiatal hernia or esophagitis with those who did not have those diagnoses. They showed that the patients with hiatal hernia had a higher rate of hospitalization with iron deficiency anaemia (hazard ratio 2.9%) than those with esophagitis alone (hazard ratio 2.2%). Though there was a higher risk of iron deficiency anaemia in those with esophagitis in the above mentioned study, it did not achieve statistical significance with 95% confidence interval (0.79-6.0). To our knowledge, there are no other studies to answer the above question. In our study, esophagitis was found in 28.2 % of our population. The prevalence of anaemia (<12 g/dl) in those with esophagitis was marginally higher than those without esophagitis in our study at 53.1% (17/32) and 52 % (39/75) respectively, after adjusting for the presence of Cameron ulcers which was not statistically significant. Our small population size might also be a contributing factor in not achieving statistical significance.

A larger patient population and a prospective study would provide further insight to the above mentioned association. However the reason for iron deficiency anaemia in those without Cameron ulcers and without esophagitis still remains unclear. Several explanations could be sought for the same as follows. One possible explanation is that these Cameron ulcers are sometimes missed during routine endoscopy as they need careful and meticulous examination with anterograde and retrograde techniques to be identified because of their difficult location and most of them are small superficial erosions. It could also be that, these ulcers exist in a continuous spectrum of healing and relapse which could theoretically explain the absence of Cameron ulcers in majority of these patient populations with large HH. We also suggest that in these patient populations with iron deficiency anaemia not explained by Cameron ulcers or esophagitis, alternative causes of IDA (Iron deficiency anaemia) should be extensively pursued. This should include other GI causes of anaemia including celiac disease, occult lower GI bleed, nutritional causes etc. and other extra intestinal causes of IDA. Our Study being retrospective in nature, it was beyond our scope to look into the alternate causes of IDA as listed above.

Limitations

Our study was done in a retrospective manner which has its own limitations. We did not have complete iron studies on all our patient population to accurately classify the type of anaemia. Our data on iron deficiency was based on the fact that we had strict exclusion criteria for other chronic causes of anaemia. Some of our patients did not have a complete endoscopic workup (small bowel capsule study/deep enteroscopy) which could overestimate the magnitude of anaemia from large Hiatal hernia alone. Because of the retrospective nature of our study it was not possible to acquire exact information on the proportion of patients who underwent small bowel study (on subsequent inpatient or outpatient basis) to evaluate other causes of GI bleed, which was a drawback in our study.

Conclusion

From our study, it is clear that the prevalence of Cameron ulcer significantly increases with the size of hiatal hernia. There is a clear association between iron deficiency anaemia and large hiatal hernia as evidenced in more than 50% of our population, however the presence of Cameron ulcers could not explain it all. Esophagitis appears to have a role in causation of anaemia; however it did not achieve statistical significance in our study. Future prospective controlled studies are warranted to analyse this further. In large HH population with IDA unexplained by Cameron ulcers and esophagitis, alternative GI (including celiac) and non-GI sources of anaemia should be extensively sought.

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