

# Prevalence of Anaemia in Patients Diagnosed with Colorectal Cancer

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## 1. Abstract

**1.1. Background:** Colorectal cancer is the fourth most common cancer and the second leading cause of cancer mortality in the UK. Colorectal cancer is rare before age 40; the incidence rises gradually to 3.7/1000 per year by age 80. Anaemia is frequently seen at presentation in colorectal cancer patients, with a reported incidence of > 30%. The incidence depends on the site of the cancer.

**1.2. Aim:** To assess the prevalence of anaemia in patients diagnosed with tumours located in different segments of the colon and rectum.

**1.3. Method:** All patients diagnosed with colorectal cancer at the Luton and Dunstable University Hospital UK from January 2015 through December 2019 were retrospectively identified from the referral database created by colorectal specialist nurses in the colorectal service. Data were retrieved by detailed review of the hospital case notes, ICE/Evolve (Computer database for investigations and correspondence) including endoscopy; radiographic imaging; operative course and cancer follow up

**1.4. Result:** In the study period 919 patients were diagnosed with colorectal cancer percentages of studied participant were Male 52.99% (487) and Female 47.00% (432). The mean age of 74.14 years (range, 25 to 101). Thirty-seven (37) (4.02%) patients were excluded from the study twenty-nine 29 (2.97%) missing data/ investigations and eight patients 8 (0.87 %), Iron deficiency present in 250 (28.3%) and 164 (18.59%) patients had Normocytic anaemia. Patients with no anaemia 53% (468 / 882) were more likely to have a diagnosis of Colorectal cancer than those who were anaemic 47% (414/882).

**1.5. Conclusion:** In Patients presenting with anaemia, examination of whole colon is mandatory because there is a greater likelihood of a cancer

in the proximal colon. Timely diagnosis and complete resection remain the keystones for the management of colon cancer.

## 2. Introduction:

Colorectal cancer is the fourth most common cancer and the second largest cause of cancer mortality in the UK. According to World Health Organization, globally, there were 1.8 million new cases and almost 861,000 deaths in 2018. In UK over 42,000 people are diagnosed with bowel cancer every year. Around one in three people who develop colorectal cancer die of this disease within five years [1]. Anaemia is often a presenting sign in colorectal cancer patients, with reported incidences of > 30% [2]. Assessment for anaemia is one of the most common problems seen in clinical practice. Though the evaluation may be straightforward in an otherwise healthy individual with a single cause of anaemia, in numerous cases the cause is not readily evident and multiple conditions may be contributing. Anaemia is thought to be more common in tumours of the proximal colon than in tumours of the distal colon and rectum [3]. Anaemia can be associated with increased postoperative morbidity and mortality [4] and is a contributing factor for poor long-term outcome, probably by aggravating tumour hypoxia. [5,6] Iron deficiency anaemia occurs as a result of chronic tumour-induced blood loss and impaired iron homeostasis. Chronic blood loss reduces iron stores and initiates absolute iron deficiency.

**Aim:** To assess the prevalence and type of anaemia in patients diagnosed with tumours located in different areas of the colon and rectum

## 3. Methods

All patients managed with colorectal cancer at the Luton and Dunstable University Hospital UK from January 2015 through December 2019 were retrospectively identified from the referral database created by the colorectal specialist nurses in the colorectal service. Data were retrieved by detailed review of the hospital case notes, ICE and Evolve (Computer database for investigations and correspondence) including endoscopy; radiographic imaging; operative course and cancer follow up. The following parameters were recorded: age, gender, source of referral, presentation, stage of the disease, MDT discussion, intervention, and outcome. Tumour locations were classified as the right colon (including caecum, ascending colon, hepatic flexure, transverse colon), left colon (including splenic flexure, descending colon, sigmoid) and recto sigmoid and rectum). Haemoglobin (Hb), mean corpuscular volume (MCV) and mean corpuscular haemoglobin concentration (MCHC) at presentation were obtained from ICE (Computer database for investigations) along with Ferritin. Anaemia was defined as Haemoglobin below the normal range of 130 g/l (Men 130 -165 g/L and Women below the normal range 120 - 155 g/L) Iron deficiency was defined as low haemoglobin with microcytosis and hypochromia with low ferritin if measured.

**Inclusion:** All patients diagnosed with colorectal cancer

**Exclusion:** Missing data/ investigation, Metastatic colorectal cancer with unknown primary site.

3.1. Statistical Analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS, version 26). Mean values were compared using the *t* test (Table 1). Univariate analysis of categorical variables was performed by the chi-square test (Table 2). Pearson’s chi squared test was used for comparing two proportions (Table 3).

The association between anaemia as a dependent variable and different explanatory variables was analyzed using a proportional odds logistic regression model. An OR with corresponding 95% confidence interval >1 implied a positive association, whereas an OR with corresponding 95% confidence interval <1 implied a negative association (Table 4). Two-sided *p* values <0.05 were considered significant.

One-Sample Test					
	Test Value = 0				
	t	df	Sig. (2-t)	Mean D	95% Confidence Interval of the Difference
					Lower
Age	149.989	881	0	6.6859	6.5985
Gender	90.953	881	0	1.5295	1.4965
Anaemia	25.159	881	0	0.6553	0.6042
cancer	100.121	881	0	1.6293	1.5973
Colon	65.077	881	0	6.7166	6.514

Table 1

	Age	Gender	Anaemia	cancer	Colon
Chi-Square	662.454a	3.066b	167.048c	58.939b	603.755d
df	7	1	2	1	8
Asymp. Sig.	0	0.08	0	0	0
a 0 cells (0.0%) have expected frequencies less than 5. The minimum expected cell frequency is 110.3.					
b 0 cells (0.0%) have expected frequencies less than 5. The minimum expected cell frequency is 441.0.					
c 0 cells (0.0%) have expected frequencies less than 5. The minimum expected cell frequency is 294.0.					
d 0 cells (0.0%) have expected frequencies less than 5. The minimum expected cell frequency is 98.0.					

Table 2

	Value	Chi-Square Tests		
		df	Asymptotic Sig.	Exact Sig. (2-sided)
Pearson Chi-Square	16.564a	1	0	
Continuity Correction	16	1	0	
Likelihood Ratio	16.583	1	0	
Fisher's Exact Test				0
Linear-by-Linear	16.545	1	0	
N of Valid Cases	882			
a 0 cells (0.0%) have expected count less than 5. The minimum expected count is 153.86.				
b Computed only for a 2x2 table				

Table 3

	Risk Estimate		
	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for cancer (Right colon / Left colon)	1.769	1.343	2.331
For cohort Gender = Female	1.339	1.167	1.536
For cohort Gender = Male	0.757	0.657	0.871
N of Valid Cases	882		

Table 4

Gender	No Anaemia	Iron def	Normocytic	Total
Female	202	124	89	415
Male	266	126	75	467
<b>Total</b>	<b>468</b>	<b>250</b>	<b>164</b>	<b>882</b>

Table 5

	Anaemia * Colon Crosstabulation								Total	
	Right Colon				Left Colon			Recto sigmoid + Rectum		
	Caecum	Ascending	Hepatic Flex	Transverse	Splenic flex	Descendn	Sigmoid	Recto sig		Rectum
Anaemia	86	58	31	29	8	19	87	15	81	414
Iron def	56	36	21	18	7	13	45	8	46	250
Normocytic	30	22	10	11	1	6	42	7	35	164
No Anaemia	57	30	17	19	8	12	117	28	180	468
<b>Total</b>	143	88	48	48	16	31	204	43	261	882
				<b>327</b>			<b>251</b>		<b>304</b>	

Table 6

4. Results

In the study period 919 patients were diagnosed with colorectal cancer. Male 52.99% (487) and Female 47.00% (432). The mean age was 74.14 years (range, 25 to 101). Thirty-seven (37) (4.02%) patients were excluded from the study. Twenty-nine 29 (2.97%) had missing data/ investigations and eight patients 8 (0.87 %), has no primary site of colorectal cancer identified (Figure: 1). 882 patients had a Full blood count measured at presentation of the suspected diagnosis. Ferritin was measured in 232 of these patients. Anaemia was evident in 46.93% (414) of all cancers. Iron deficiency was present in 250 (28.3%), 164 (18.59%) patients had a normocytic anaemia (Table 5). [Patients with no anaemia 53.06% (468) were more likely to have a diagnosis of Colorectal cancer than those who were anaemic 46.93% (414)]. In the Right colon subset of patients there was a total of 327 patients (144 male and 183 female). Anaemia was present in 9.75% (86) in the caecum, 6.57% (58) Ascending

colon, 3.51% (31) Hepatic flexure, and 3.28% (29) Transverse colon. of these 123 (37.61%) had a normal hemoglobin and 204 (62.38 %) had a low haemoglobin. Of these anaemic patients 131 (37.00%) had low MCV/ MCH and 27 (8.25%) low ferritin suggesting an iron deficiency anaemia. So, of the 327 (37.07%) patients diagnosed with a Right colon tumour, 204 had anaemia at presentation with 40.06% (131) of these being iron deficient (Figure: 2). In 251 patients with left colon cancer, Anaemia was present in 0.90% (8) in the splenic flexure, 2.15% (19) Descending colon and 9.86% (87) in the Sigmoid colon. In the left colon cancer 137 (54.58%) had normal haemoglobin and 114 (45.41%) were anaemic, 49 (19.52%) of these were normocytic and 65(25.89%) had an iron deficiency anaemia. Of 304 rectosigmoid and rectal cancer patients anaemia was present in 1.70% (15) in the rectosigmoid and 9.18% (81) in the rectum. In the rectosigmoid and rectum cancer 208 (68.42 %) had a normal haemoglobin. 96 (31.57%) were anaemic at presentation with

54 (17.76%), of these having iron deficiency anaemia. 42 (13.81%) had normocytic anaemia. In summary Right colon cancer patients anaemia was present in 37.07%. Those presenting with a Left colon cancer, 28.45% were anaemic, and patients with rectosigmoid and rectum cancers anaemia was present in 34.46%. (Figure: 2, Table 6). In this cohort, the prevalence of anaemia rose with age, the highest prevalence being in the >70 s. (Figure:3)

## 5. Discussion

Colorectal cancer is a major health problem. It is well recognized that anaemia is presenting sign in colorectal cancer. Colorectal cancer may present with Iron deficiency anaemia [7-9] Anaemia is an indicator of cancer risk, [10] and iron deficiency anemia is a significant contributor, accounting for 50% of all causes of anaemia [11] Iron deficiency anaemia is not a disease in itself, but is a manifestation of underlying disease such as malignancy. Searching for causes of iron deficiency anemia is therefore crucial. Patients with colon cancer experience chronic low level gastrointestinal bleeding, potentially causing iron deficiency anemia [12]. Evaluation for anaemia is one of the most frequent tests in clinical practice. In patients with iron deficiency anaemia, haemoglobin, MCV and MCH typically decrease in parallel. Evaluations of Red Blood Cell (RBC) indices, mean corpuscular value (MCV) Mean cell Haemoglobin (MCH), Mean cell Haemoglobin Concentration (MCHC) are integral part of determining the cause of anaemia. Iron deficiency anaemia is often asymptomatic, as blood loss is slow and chronic [13] The aim of investigating iron deficiency anaemia is to seek out pathology in the gastrointestinal tract, especially malignancies [14]. The World Health Organization defines anaemia as a haemoglobin concentration below 13 g/dl in men over 15 years of age, below 12 g/dl in non-pregnant women over 15 years of age, and below 11 g/dl in pregnant women [15]. The diagnostic criteria for anaemia in iron deficiency vary between published studies [16-21] The normal ranges for haemoglobin also varies between different populations in the UK. In our institution the normal range of haemoglobin in (Men is 130 -165 g/L, and the Women 120 – 155 g/L) (MCV 80 – 100 fl, MCHC 280 – 355 g/L, Ferritin 30 – 400 ng/mL).

In this study the lower limit of the normal range for the laboratory performing the test was used to define anaemia. The NICE referral guidelines for suspected lower GI cancer suggest that only patients with haemoglobin concentration <11 g/dl in men or <10 g/dl in non-menstruating women be referred [22]. It has been suggested that these cut-off values miss patients with colorectal cancer, especially men [23]. In our cohort Patients with no anaemia 53.06% (468 /882) were more likely to have a diagnosis of Colorectal cancer than those who were anaemic 46.93% (414/882), and the proportions of anaemic patient was slightly higher in tumours of the distal than tumours in the proximal colon. This is in contrast to study of Dunne JR et al and other published studies. Prevalence rate of anaemia in our study was 46.93%. This is similar to other published studies. In our study the prevalence rate of anemia rises more rapidly from middle age and has a higher prevalence rate in aged >70 years. These findings are comparable to other published studies [34]. Prevalence rates of anaemia in older adults were found to vary between 2.9 and 51 percent in men and 3.3 and 41 percent in women [24,34] While nursing home residents were found to be at high risk for anaemia, [25,26] the highest prevalence rates were noted in hospitalized older adults [27,34]. This is similar to our study. Several randomized controlled trials [28,29] have revealed that survival in patients with colorectal cancer is

considerably better when the diagnosis is made at an early stage, making a convincing case for early detection through screening programs [30] However, most patients with colorectal cancers are diagnosed after the onset of cancer-related symptoms [31] and it is imperative that frontline providers recognize early diagnostic clues to colorectal cancer. Studies have shown that rectal bleeding as an initial presentation of colon cancer and are associated with an early stage of the disease and better survival [32,33]. In this study, the numbers of men diagnosed with iron deficiency anaemia were slightly higher to that of women diagnosed with iron deficiency anaemia. The mean age of the patients with anaemia was 74.44 years; the majority of them were between 70 - 89 years of age. These findings comparable to study of Guralnik et al in which prevalence rate of anaemia was highest in men aged > 85 years, [34] and in contrast with study of Looker et al in which iron deficiency anaemia was more prevalent in women of childbearing age [35]. Iron deficiency anaemia has a higher PPV. A case –control study by Hamilton et al found that the PPV of a Haemoglobin <11 in men and <10 in women for CRC was 13.3% and 7.7% respectively in the over 60s age group [36]. This study suggests that any anaemia (haemoglobin) below 120 g/l should be investigated. This is similar to other published studies [37]. Simpler guidance would be to ignore features of iron deficiency entirely and recommend urgent referral of patients over 60 with unexplained anaemia on the haemoglobin value alone. If this were done, the current threshold figures of 110 g/l [37] for men and 100 g/l [37] for women appear reasonable. Colorectal cancer generally presents with low-risk symptoms, so if earlier symptomatic diagnosis is to be achieved, lower specificity cannot be avoided. This study estimates the risk of colorectal cancer across different ages, gender, and levels of haemoglobin and endorses the convincing relationship between cancer and anaemia. The results can be used to guide in deciding whether to refer patients with an abnormal haemoglobin results; they can also be used to improve guidelines.

One of the strengths of our study is that the sample size is not small. The limitations of this study were availability of blood tests results and some missing notes/data.

## 6. Conclusion

We recommend, in patients presenting with anaemia, examination of the whole colon is to be recommended as likelihood of a cancer in the proximal colon. The more proximal the tumour, the more likely likely the patient is anaemic. Timely diagnosis and complete resection remains the keystones for the management of colon cancer.

919 Study Patients		
29 Missing data & 8 no primary tumour identified (Excluded 37)		
882 Studied patients		
468(53.06%) Anaemia	No	414 (46.93%) Anaemia
250 Iron deficiency		164 Normocytic

Figure 1

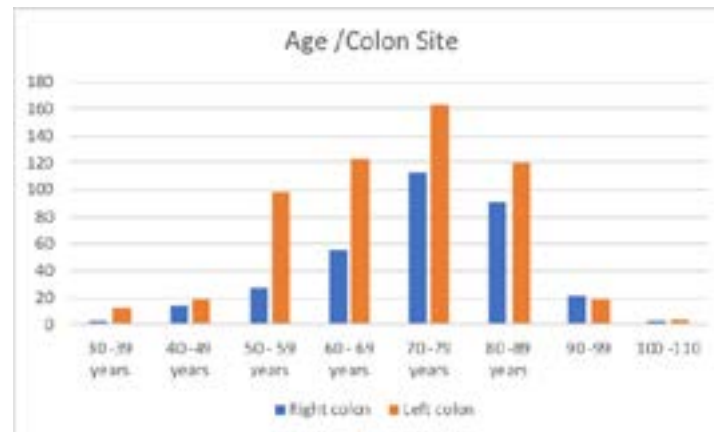


Figure 2

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