Retrospective Study

Retrospective study of colorectal cancer in Zimbabwe: Colonoscopic and clinical correlates

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Abstract

AIM: To compare differences in the frequency of colorectal cancer at colonoscopy in Zimbabwe according to ethnicity.

METHODS: All lower gastrointestinal endoscopic procedures performed between January 2006 and December 2011 at a gastroenterology clinic in Harare, Zimbabwe were reviewed. The demographic characteristics, clinical indications, differences in bowel preparation and the endoscopic and histological diagnoses were compared between different ethnic groups with emphasis on colorectal cancer. The clinical and demographic characteristics and the endoscopic findings were compared using the student t-test and the χ² test, while the clinical indications associated with a diagnosis of colorectal cancer were determined by logistic regression.

RESULTS: All colonoscopies and sigmoidoscopies performed in 1236 Caucasians, 460 black Africans and 109 Asians were analysed. Colorectal cancer was diagnosed more frequently in the black African patients compared to Caucasians or Asians (10% vs 3%, 10% vs 2%, P < 0.001). However, polyps were less common among black Africans (5%) compared to both Caucasians (8%) and Asians (9%) (P = 0.03). Among patients with colorectal cancer, black Africans tended to be younger than Caucasians, who were over-represented in the oldest age category; 32 % vs 2% were less than 50 years and 41% vs 78% were older than 60 years (P < 0.001). Anaemia and weight loss were associated with colorectal cancer in both black African [odds ratio (OR): 2.73 (95%CI: 1.33-5.61) and 3.09 (1.35-7.07)] and Caucasian patients [OR: 6.65 (95%CI: 2.93-15.09) and 3.47 (1.52-7.94)].

CONCLUSION: The likelihood of diagnosing colorectal cancer in patients referred for colonoscopy in Zimbabwe is at least as likely among black Africans as it is among Caucasians.

Key words: Colorectal cancer; Africa; Epidemiology; Colonoscopy; Adenomatous polyps; Diverticulosis; Colitis
INTRODUCTION

Traditionally, colorectal cancer was regarded as an unimportant problem in Africa, even though the condition is associated with a high mortality rate\(^1\). The 5-year survival rate among Ugandan and Zimbabwean patients diagnosed between 1993 and 1997 was 8.3\(^\%\)\(^2\) and 17.4\(^\%\)\(^3\) respectively. This is worse than the 5-year survival rate in England and Wales in 1971-1975 which was 22.0\(^\%\), and which is currently 54.4\(^\%\)\(^4\). Survival is even better in the United States at 64\(^\%\)\(^5\). The poorer outcome of patients with gastrointestinal cancers in Africa is partly due to delays in presentation and diagnosis\(^2\). Furthermore, many patients do not receive appropriate treatment even after diagnosis due to limited resources, whilst others prefer traditional or faith-based remedies. These delays probably result from the perception by clinicians that colorectal cancer is a rare condition, coupled with lack of awareness by the populace.

Available evidence from cancer registries supports the perception that colorectal cancer is rare in Africa\(^6\). The age-standardised incidence per 100000 ranges from as low as 1.5 in males and 2.5 in females in the Gambia to 8.5 in males and 7.1 in females in Zimbabwe\(^1\). In contrast, the age-standardised incidence rate per 100000 among Caucasians in Zimbabwe is much higher at 49.8 and 35.5 in males and females respectively\(^1\). This is comparable to the average age-standardised incidence rate in the developed world of 37.6\(^6\).

Part of the difference in incidence between Caucasians and black Zimbabweans may be explained by differences in health seeking behaviour and access to comprehensive health services. The apparent rarity could then reflect a reduced capacity to ascertain the diagnosis among black Zimbabweans. This would be consistent with isolated reports suggesting that colorectal cancer occurs more frequently among blacks in Africa than commonly assumed\(^7\). However, the prevailing opinion is that it is a rarity\(^9\).

The apparent rarity of colorectal cancer in Africa has been attributed to either protective dietary factors such as a high fibre diet or the absence of known risk factors such as dietary animal protein and fat but the specific influences are subject to debate\(^10\). African communities are gradually adopting lifestyles that are similar to those of more affluent societies, which report a much higher incidence of colorectal cancer\(^11\). If these lifestyles are aetiological, then one would expect a rising incidence of colorectal cancer in parts of Africa. Moreover, colorectal cancer is a leading cause of cancer-related deaths among African-Americans, who share some genetic characteristics with African communities\(^12\). It is therefore reasonable to expect a higher prevalence of colorectal cancer in Africa than previously reported.

A demonstration that colorectal cancer is more frequent than commonly assumed might lead to a reappraisal of clinical practice, medical priorities and resource allocation. Zimbabwe has different racial groups, which have differences in the risk factors associated with colorectal cancer. The incidence of colorectal cancer is different between the various racial groups, being regarded as much more common among Caucasians. This study compared the frequency and the clinical features of colorectal cancer between different racial groups presenting for colonic evaluation at a gastroenterology unit in Harare, Zimbabwe. Secondly, the study also sought to identify common conditions diagnosed on colonoscopy or sigmoidoscopy in patients presenting for these procedures in different racial groups.

MATERIALS AND METHODS

Patients and setting

All lower gastrointestinal endoscopic procedures (colonoscopy and sigmoidoscopy) performed between January 2006 and December 2011 at an endoscopic unit in Harare, Zimbabwe were reviewed. The unit performs between 200 and 600 lower gastrointestinal procedures annually. It was the only unit in Zimbabwe offering a regular colonoscopy service for most of the period under review. The patients were referred from primary care physicians, various clinical specialties, and both public and private hospitals. All patients older than 16 years of age who had a colonoscopy or sigmoidoscopy within the period were eligible for the review. Repeat procedures within the study period were excluded, unless if there was an important new finding or if the procedure was repeated because the
initial evaluation was inadequate. In the later scenario, the initial inadequate evaluation was excluded from the review.

Procedures
A manual search of the records of all lower gastro-intestinal procedures was carried out after approval from the institutional ethics review committee. All procedures had been performed by one of the authors (Gangaidzo IT) using Olympus CIF30L fibrosopes or EV206 videoscopes. Informed written consent for the procedures had been obtained as per standard clinical practice. The patient details, clinical indications, procedures and findings were recorded onto a standard report form. One of three methods of bowel cleaning was used, namely oral mannitol 20% solution, or either of two proprietary sodium phosphate-based preparations, Fleet Phosphosoda® or Coloprep®. All three methods involved high fluid intake of at least 4 litres. A split-dose regimen was utilised, commencing on the day before the procedure and concluding on the morning of the procedure. Patients with a poor bowel preparation proceeded to full examination with the aid of colonic irrigation. In a very small proportion, this proved inadequate and the procedure was rescheduled following a repeat bowel preparation.

All patients were examined under conscious sedation following the administration of variable amounts of midazolam and pethidine. No patient was examined whilst fully awake or under general anaesthesia. Intubation of the caecum was the primary objective during colonoscopy, but ileal intubation was attempted where clinically indicated. Abnormalities were regarded as significant if they led to further specific investigations or treatment. A biopsy was taken if there were macroscopic abnormalities, or if there was a clinical indication. A polypectomy using snare diathermy was undertaken when indicated. All histological evaluations were done by one of three experienced pathologists. The patients were usually discharged on the same day, a few hours after recovery.

Statistical analysis
Demographic data, indications for the procedure, family history of bowel cancer, method of bowel preparation, the extent of the procedure and the endoscopic findings were abstracted from the reports. Pathology reports generated by one of two laboratories were obtained from patient files. Statistical analyses were performed using STATA/MP version 12.0 (College Station, Texas, United States). Demographic characteristics, details of the procedures, indications and findings were compared between racial groups using the $\chi^2$ test for categorical variables and the Student $t$-test for continuous variables. A $P$ value of less than 0.05 was considered significant. Multivariate logistic regression was performed to determine the clinical features associated with colorectal cancer in blacks Africans and Caucasians. The dependent variable was colorectal cancer and the independent variables were the indications for the procedures including routine screening, haematochezia, anaemia, change in bowel habit, loss of weight, abdominal pain and a family history of colorectal cancer.

RESULTS
A total of 1866 colonoscopies and 32 sigmoidoscopies performed in the 6-year period ending December 2011 were considered for analysis. Of these, 93 were repeat examinations within the period and were excluded from analysis. As a result, 1805 procedures were analysed.

Table 1 shows the patient demographics and details of the procedures. There were 1236 Caucasian patients, 460 black African patients and 109 patients of Asian origin. The mean age at colonoscopy was significantly lower in black patients (Table 1) compared to both Caucasians and Asians ($P < 0.001$). There were no differences in the bowel preparation regimens used across the three groups, but the resulting quality of bowel preparation was worse among black Africans compared to other ethnic groups ($P < 0.001$).

Indications for lower GI endoscopy
Some patients had more than one indication or symptom on presenting for a colonic procedure (Table 2). The most common indications were a change in bowel habit (43%), abdominal pain (26%) and rectal bleeding (24%). Rectal bleeding was more common as a reason for undergoing colonoscopy in black African patients (38%) than in Caucasians (19%) and Asians (20%). Anaemia was a more common indication for colonoscopy among black Africans (15%) and Asians (16%) than among Caucasians (4%). Conversely, black African patients were less likely to present for mere screening in the absence of symptoms. Of the 31

| Table 1 Patient demographics, differences in bowel preparation and extent of examination | $n$ (%) |
|---------------------------------|--------|
| Variable                        | Black Africans | Caucasians | Asians/other | $P$ value |
| Sex                             | $n = 460$ | $n = 1236$ | $n = 109$    |          |
| Male                            | 242 (53)  | 605 (49)  | 51 (47)      |          |
| Female                          | 218 (47)  | 631 (51)  | 58 (53)      | 0.332    |
| Age (yr) mean ± SD              | 55 (16)   | 60 (13)   | 58 (15)      | < 0.001  |
| Bowel preparation regimen       |          |          |              |          |
| Mannitol 20%                    | 161 (37)  | 516 (42)  | 516 (42)     |          |
| Fleet phosphosoda               | 259 (59)  | 687 (56)  | 682 (56)     |          |
| Coloprep                        | 16 (4)    | 30 (2)    | 30 (2)       | 0.314    |
| Result of bowel preparation     |          |          |              |          |
| Poor                            | 84 (18)   | 134 (11)  | 14 (13)      |          |
| Good                            | 200 (44)  | 520 (42)  | 40 (37)      | < 0.001  |
| Excellent                       | 176 (38)  | 588 (47)  | 55 (50)      |          |
black African patients who presented for a screening colonoscopy, 6 had a family history of bowel cancer. In contrast, 331 (27%) Caucasian patients had a screening colonoscopy, 40% of whom reported a family history of bowel cancer.

**Endoscopic and histological diagnoses**

Tables 3 and 4 show the diagnosis following colonoscopy or sigmoidoscopy in different races. Colorectal cancer was found in a greater proportion of black African patients compared to Caucasian and Asian patients (10% vs 3%, 10% vs 2%, \( P < 0.001 \)). Moreover, colorectal cancer occurred at an earlier age among the black African patients (Table 5). Four black African patients with colorectal cancer were below 40 years of age; the youngest was 19. These four all had tumours distal to the splenic flexure. Of these four tumours, 2 were adenocarcinomas, one a signet ring cell carcinoma and the other one a mucinous adenocarcinoma. Thirteen (30%) of the black patients with colorectal cancer were below 50 years of age. In contrast, the youngest Caucasian patient was 50 years old. Caucasian patients with colorectal cancer tended to be much older than black African patients - 78% vs 41% were older than 60 years (\( P < 0.001 \)).

The tumour was proximal to the splenic flexure in 39% of black patients compared to 27% of Caucasian patients, but this difference was not statistically significant. Polyps were uncommon among black African patients examined (4%), even though colorectal cancer was frequently diagnosed in this ethnic group. The other tumours diagnosed at colonoscopy were a B-cell lymphoma of the MALT type in a Caucasian patient and a diffuse large B-cell lymphoma and Kaposi sarcoma in two black African patients.

Colitis was also diagnosed in a greater proportion of black African patients compared to Caucasians (7% vs 2%, \( P < 0.001 \)). The underlying causes of colitis included inflammatory bowel disease, infections, irradiation, non-specific colitis and microscopic colitis. There was one black patient with tuberculosis of the caecum and terminal ileum. Inflammatory bowel disease was diagnosed in 9 (1%) Caucasian patients, 8 (2%) black African patients and 1 Asian patient. Diverticular disease was less common among black Africans compared to Caucasians (6% vs 28%, \( P < 0.001 \)). There was no change in these results when asymptomatic patients, who had presented for a screening colonoscopy, were excluded from analysis.

**Associations of colorectal cancer**

Certain indications for the procedure were more likely to be associated with a subsequent diagnosis...
of colorectal cancer (Table 6). Anaemia and loss of weight were highly associated with colorectal cancer in both black African [odds ratio (OR): 2.73 (95%CI: 1.33-5.61) and 3.09 (1.35-7.07)] and Caucasian patients [OR: 6.65 (95%CI: 2.93-15.09) and 3.47 (1.52-7.94)]. Rectal bleeding was associated with colorectal cancer in Caucasians [OR: 2.44 (95%CI: 1.26-4.75)] but not in black Africans [OR: 1.69 (95%CI: 0.89-3.24)]. We found no statistically significant association between a family history of bowel cancer and a diagnosis of colorectal cancer in black Africans [OR: 3.13 (95%CI: 0.61-16.03)] or Caucasians [OR: 1.12 (95%CI: 0.26-4.82)].

**DISCUSSION**

This study demonstrated that the likelihood of diagnosing colorectal cancer in patients referred for colonoscopy is, at the very least, as likely among black Africans as it is among Caucasians. Indeed, colorectal cancer was diagnosed more frequently among black African patients compared to Caucasians, who would be expected to have a higher burden of the disease. However, adenomatous polyps were found more frequently in Caucasian patients. Various forms of colitis were also diagnosed more frequently among black Africans than both Caucasian and Asian patients. A higher than expected proportion of black African patients (7%) had diverticular disease, even though this was still considerably lower than in Caucasian patients (29%).

These results are a striking departure from the traditional thinking that colorectal cancer is a rarity in Africa. Admittedly, the motivation for seeking a colonoscopy was different between the groups. A higher proportion of black Africans (38%) were referred for evaluation of haematochezia compared to Caucasians (19%) and Asians (20%). Similarly a higher proportion of Africans (15%) were referred because of anaemia compared to Caucasians (4%) although not when compared to Asians (16%). Conversely, a higher proportion of Caucasians were referred for a screening colonoscopy. However, the impact of these differences on the results is minimal, since colorectal cancer remained more frequent among black Africans when all patients who came for screening were excluded from analysis.

The high colorectal cancer burden in the black African patients in our study is consistent with the few reports suggesting that that colorectal cancer is on the rise in Africa. There was a 3-fold increase in the number of patients diagnosed with colorectal cancer at a single referral unit in Kenya between the periods 1993-1998 and 1999-2005. Recent data from the Zimbabwean cancer registry suggested that the incidence of colorectal cancer in Harare has been rising between 1991 and 2010. Furthermore, the incidence of colorectal cancer among Africans appears to be higher in Zimbabwe and South Africa compared to other sub-Saharan African countries. This is likely to be due to differences in health systems and the capacity to report cases adequately rather than a truly higher incidence of colorectal cancer.

The results also demonstrate the occurrence of colorectal cancer at an earlier age among Africans compared to Caucasians. It can be argued that this is a result of different population age structures between the major ethnic groups in this study. However, an earlier age of onset has been demonstrated not only in other African studies, but also among African-Americans. It is plausible that the young African patients have an underlying genetic predilection, and that colorectal cancer develops in these patients through unique pathways. Conversely, it is possible that these young patients may have been exposed to unique occupational and other environmental carcinogens, since they comprise the working population.

The low prevalence of polyps among Africans despite a high frequency of colorectal cancer in this cohort is also a possible pointer towards the existence of such pathways. Adenomatous polyps have been reported to be rare among Africans, and hitherto, this has been assumed to reflect the low background prevalence of colorectal cancer. The low rate of polyps among black Africans in our study could reflect an alternative mode of carcinogenesis other than the traditional adenoma-carcinoma sequence. Alternatively this could also be simply a consequence of the younger age of black Africans presenting for colonoscopy, along with the poorer bowel preparation.

Another intriguing finding of our study was that diverticular disease, though less common than in Caucasians, was present at a higher than expected frequency among black African patients. Like colorectal cancer, diverticular disease is considered rare in Africa. This observation formed the basis of the theory that a high-fibre diet, as traditionally consumed in Africa, reduces the risk of large bowel diseases, including diverticular disease and colorectal cancer. If this is correct, then the relatively higher than expected frequency of diverticular disease could reflect a change in the epidemiology of large bowel diseases in Zimbabwe, possibly as a result of changes in dietary habits. However, it can also be argued that the poorer quality of bowel preparation in black Africans in our

| Table 6 Predictors of colorectal cancer |
|---------------------------------------|
| **Symptoms**                          | **Adenocarcinoma (n = 44) OR (95%CI)** |
|                                       | **Black Africans (n = 413)**       | **Caucasians (n = 831)**       |
| Haematochezia                          | 1.69 (0.89-3.24)                  | 2.44 (1.26-4.75)               |
| Change in bowel habit                  | 0.85 (0.45-1.58)                  | 0.93 (0.47-1.82)               |
| Abdominal pain                         | 0.87 (0.45-1.75)                  | 0.71 (0.33-1.54)               |
| Anaemia                                | 2.75 (1.33-5.61)                  | 6.65 (2.93-15.09)              |
| Loss of weight                         | 3.09 (1.35-7.07)                  | 3.47 (1.52-7.94)               |
| Family history                         | 3.13 (0.61-16.03)                 | 1.12 (0.26-4.82)               |

1Multivariate analysis of clinical predictors of colorectal cancer.
study could reflect consumption of a high-fibre high-residue diet, implying that current dietary patterns are still substantially “traditional” and presumably “protective”. The differences in quality of bowel preparation could also be due to cultural differences in how instructions for bowel preparation are perceived and followed.

While this study has some limitations, it is a reflection of clinical practice in Zimbabwe. Inferences to the general population should be drawn cautiously, given that these patients had clinical indications for colonoscopy in most instances. It can also be argued that proximal lesions could have been missed in the few patients who had flexible sigmoidoscopy. However this is unlikely as sigmoidoscopy was usually performed only when the clinical picture was overwhelmingly suggestive of an accessible distal lesion. There were also differences in the indications for colonoscopy and access to the procedures was potentially limited by user fees. This could have introduced selection bias, as patients from a higher socio-economic stratum could have been over-represented. However, colorectal cancer has hitherto been considered rare in blacks in Africa, even the affluent, thus this does not really affect the implications of these results. Moreover, the patients in this study came from a wide-spectrum of the populace, including public hospitals, therefore diluting potential selection bias. While it was not possible to obtain precise measures of incidence among the different groups from the data, the results provide a unique perspective regarding the relative frequency of colorectal cancer in a sub-Saharan African country. Although this was a single centre study, it accounted for more than 60% of all colonoscopic examinations performed during the period under review. Thus the study is fairly representative of the Zimbabwean population undergoing colonoscopy. Moreover, all the procedures were done by an experienced gastroenterologist. The caecal intubation rate averaged 88.3%, but this is a crude estimate which includes instances where the examination was not completed because of poor preparation, colonic stenosis from tumours and other patient factors. Similarly, the overall adenoma detection rate was lower than recommended, but this is probably because our calculations included patients younger than 50 years. In any case, even if one were to assume that some lesions were missed, this should not differ between races. If at all some lesions were missed, it would be more likely to be in the black Africans who tended to have poorer bowel preparation. In this case, then our findings would represent the tip of the iceberg, with many more adenomas among black Africans going undiagnosed.

In conclusion, colorectal cancer is an emerging challenge among black Zimbabweans, and should be considered as part of the differential diagnosis in all patients with large bowel symptoms. Extra attention should be given to those patients with anaemia and loss of weight in the appropriate clinical context. The disease can present at a relatively young age, and thus young patients with the right clinical picture should be investigated just as thoroughly as older patients. The study also provides a baseline for prospective, hypothesis driven studies, particularly among these young patients.

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