



## **Perspectives Associated with an Increase in the Incidence of Colorectal Adenocarcinoma in Uganda**

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### **Author's contribution**

*The sole author designed, analysed, interpreted and prepared the manuscript.*

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### **ABSTRACT**

This paper is a current review of work done on colorectal adenocarcinoma in Uganda highlighting the perspectives in the increased rate of cases observed in our hospitals. A steady increase of CRC in other Sub-Saharan African countries is currently being documented however this is associated with a higher CRC-associated morbidity and mortality. Reasons behind this increase may be the nutrition transition in Sub-Saharan Africa characterized by decreased consumption of dietary fibre, starch and plant proteins to a Western diet associated with consumption of fatty foods and red meat. The emergence of noncommunicable diseases such as diabetes and obesity coupled with increased alcohol consumption and smoking confers a higher risk to CRC. A shift in the demographics is observed in Uganda compared to high income countries with 22.8% of our CRC cases being diagnosed at <40years of age compared to 3-7% in high income countries. A challenge experienced with this early age onset is that it is associated with an aggressive biological behavior with a poor prognosis. The high proportion of left sided colon and rectal adenocarcinoma in Uganda makes our population more amenable to screening. However challenges experienced in Uganda and other Sub-Saharan African countries include the availability of endoscopic training and equipment, costs, availability of pathologic services and patient acceptance. The increased diagnosis of CRC cases that will result from screening will eventually require a parallel increase in

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surgical and oncological infrastructure to manage CRC patients. An improvement in diagnosing, screening and treating CRC by increasing surgical and endoscopic capacity with the aid of international medical and surgical societies should be a public health priority in Uganda given the observed epidemiological shifts. Future implementation of National screening programmes to detect CRC at an early stage is also necessary to reduce the mortality in the Ugandan population.

**Keywords:** *Low income countries; high income countries; Uganda; colorectal adenocarcinoma; screening; colonoscopy; epidemiological shifts; increased incidence; perspectives; challenges.*

**1. INTRODUCTION**

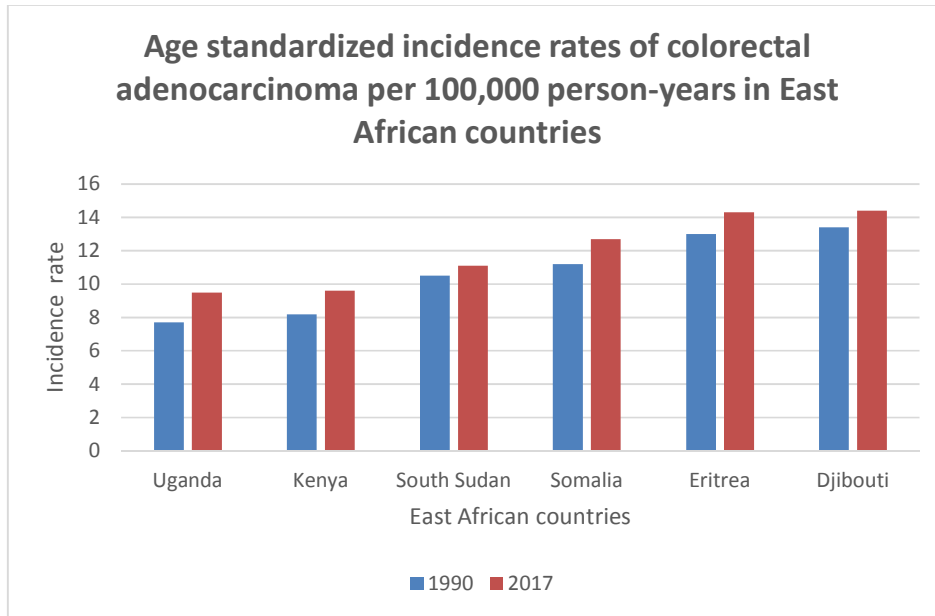
In low and middle income countries the incidence and mortality of CRC is increasing whilst some high income countries have shown a decline [1]. In Sub-Saharan Africa, CRC was previously considered to be an uncommon diagnosis due to the consumption of a high fibre diet [2]. CRC is currently the fifth most common cancer in Sub-Saharan Africa, according to the International Agency for Research on Cancer and the American Cancer Society [3].

The Kampala Cancer Registry in Uganda has registered a steady increase in the burden of CRC. In males, the age-standardized rate for CRC increased from 7.8 cases per 100,000 people per year (between 1991-1995) to 8.8 cases per 100,000 people per year (between 2006-2010). Whilst in females the age-

standardized rate for CRC increased from 5.2 cases per 100,000 people per year (between 1991-1995) to 8.8 per 100,000 people per year (between 2006-2010). Similar increases in incidence rates have been reported in other Sub-Saharan African countries. Between 1993 and 2005 in Kenya, Saidi et al, reported a 2.7 fold increase in the incidence of CRC [4].

The increase in the percentage change in age-standardized incidence rates in East African countries between the year 1990 and the year 2017 is 22.1% in Uganda, 17.5% in Kenya, 5.7% in South Sudan, 13.6% in Somalia, 14.3% in Eritrea and 7.2% in Djibouti [5].

Fig. 1 shows a bar chart depicting the steady increase in incidence in Uganda and other East African countries over the last few decades.



**Fig. 1. A bar graph showing the age standardized incidence rates of colorectal adenocarcinoma per 100,000 person-years in Uganda and other East African countries depicting a steady increase in the incidence of CRC between the years 1990 to the year 2017**

The Surgical community in the Western world should no longer assume that CRC is uncommon in Uganda and other Sub-Saharan African countries. In resource limited settings in Uganda this has implications on how to prioritize the management and early diagnosis of CRC.

This paper reviews the possible reasons behind the increased incidence of CRC in Uganda, differences in tumor location compared to the Western world and the challenges encountered in obtaining an early diagnosis of CRC in Ugandan patients.

## **2. DISCUSSION**

### **2.1 Possible Reasons Behind the rise in Incidence of CRC in Uganda**

Many authors in Sub-Saharan Africa observed an increase in the incidence of CRC which may be due to an actual increase or due to greater awareness to present to hospital with signs and symptoms of CRC in our patient population, increased specialist referrals to hospital or a better reputation for CRC management in our hospitals. More hospital admissions have been registered in Referral Hospitals in Central Uganda in the last 10 years however a higher rise in CRC has been observed [6]. The increasing prevalence and incidence of CRC is part of an on-going epidemiological shift in Sub-Saharan Africa with a rising burden from non-communicable diseases to a reduction in burden from infectious communicable diseases [7,8].

In a more global world, the introduction of a Western diet with a high consumption of red processed meat or high glycaemic load carbohydrates with low intake of fruits and vegetables coupled with rising obesity, alcohol consumption and cigarette smoking may result in an increased risk of CRC in low middle income countries to the level seen in high income countries [4,9-12]. It is difficult to unravel the relative contributions and interactions of each of these factors to an increased risk of CRC. As higher incomes are associated with a change in diet, it does not imply that this westernized diet is causative [11]. Steadily developing incomes result in a western-style diet which leads to a greater exposure to typical risk factors. In Sub-Saharan Africa there is growing need to evaluate the possible causes for the increased rates of CRC and hospitals should be well equipped and health workers should be trained and prepared to

deal with the increasing burden of CRC in Sub-Saharan Africa.

### **2.2 Limitations and Challenges in Determining the Burden of CRC in Uganda**

A limitation of conducting research in resource limited settings lies in the difficulty in reviewing medical records and obtaining complete data [13,14]. The data obtained from the Kampala Cancer Registry includes only pathologically-diagnosed cases and this leads to an underestimation in the true incidence. However, over the last three decades, the experience from the Kampala Cancer Registry has been very similar to comparable settings in Sub-Saharan Africa despite these limitations.

Resource limited institutions should be included in discussions regarding improvement of CRC care on a global level even with these expected limitations. Referral Hospitals in central Uganda still maintain written and not electronic records, hence reducing on the completeness of these medical records. The records have no ICD coding of diseases to allow for clinically-diagnosed cases and just include pathologically confirmed cases. The data from the Kampala Cancer Registry does not include premalignant lesions such as adenomatous polyps which are removed at colonoscopy. Sharing of data electronically between the Referral Hospitals in Central Uganda performing colonoscopy procedures and the Kampala Cancer Registry would be useful to benefit future studies on CRC in Uganda.

### **2.3 Change in the Demographics of CRC in Uganda Compared to the Western World**

Compared to high income countries, a younger age at CRC diagnosis has been reported in low income countries in Sub-Saharan Africa [9,15,16]. Reports from hospitals in Sub-Saharan Africa have shown that about 19-38% of CRC cases are less than 40 years of age [9]. Our experience in Uganda, has shown that 22.8% of our CRC cases are under 40 years of age compared to only 3-7% in high income countries [17,18]. 51.1% of CRC patients in Uganda are diagnosed below 54 years of age in Uganda whilst in the USA only 17.4% of CRC tend to be diagnosed below 54 years of age. From the experience of the author the youngest age seen

in Uganda was a referral of a 16 year old with rectal carcinoma.

In the UK only 16% of CRC patients had CRC diagnosed under 60 years of age [19-22]. A distinct molecular profile of CRC may be the reason for the rising prevalence and incidence of CRC in young patients [23,24]. This makes treatment of CRC in low income countries challenging as younger CRC patients have a higher stage at presentation with increased frequency of metastasis associated with a poor prognosis [18,25,26].

The epidemiology of CRC in Sub-Saharan Africa is therefore showing a shift towards an increased prevalence and incidence in patients <50 years of age [27,28]. This onset at an early age is associated with an aggressive biological behavior of CRC with a poor prognosis.

In Uganda, the greater increase in the incidence of CRC in female patients compared to male patients registered in the Kampala Cancer Registry between the years 2006-2010 may be due to differences in risk behaviors such as smoking, alcohol intake, physical activity and different levels of health awareness.

#### **2.4 Differences in CRC Location between Uganda and the Western World**

A significant difference in the location of CRC is evident between cases in low income countries compared to high income countries. Studies from Sub-Saharan African countries have shown a higher proportion of rectal and distal colon cases than those reported from high income countries [29]. Over the last 10 years we have found that the topography for CRC in Uganda is 49.4% rectum; 2.8% rectosigmoid; 24.7% sigmoid colon; 7.3% descending colon; 2.8% transverse colon; 8.5% ascending colon and 4.5% in the caecum. Therefore there is a high proportion of left sided colon cancers and rectal cancers in Uganda similar to other Sub-Saharan African countries and in contrast to that found in high income countries.

Right sided colon cancers tend to grow to a larger size before symptoms develop whilst rectal and left-sided colon cancers tend to be symptomatic presenting with large bowel obstruction, colicky abdominal pain and/or haematochezia. Screening facilities in hospitals in Uganda currently do not perform routine screening for CRC. However, in low income

countries, mathematical modeling studies have shown that CRC screening in Sub-Saharan Africa is cost effective in combating CRC [30,31].

There are several factors limiting the widespread use of colonoscopy especially in rural parts of Uganda and Sub-Saharan Africa and these include the availability of endoscopic training, costs, availability of pathologic services and patient acceptance. An increased diagnosis of CRC cases will result from screening however this will then eventually require a parallel increase in surgical and oncological infrastructure to manage CRC patients. Globally colonoscopy services are cost prohibitive and hospitals in Sub-Saharan Africa should recognize that if colonoscopy equipment is not serviced and maintained regularly then patient safety may become a concern.

In Uganda as in other Sub-Saharan African countries, screening services and endoscopic capabilities are limited and hence there is need for development of adequate infrastructure and training in this area [32]. Currently a few hospitals in central Uganda are training endoscopists to perform routine procedures and therapeutic procedures such as polypectomy during colonoscopy. However in order to meet demands these efforts need to be scaled up especially in the Referral Hospitals. In rural parts of Uganda there could be a potential benefit in training nurse endoscopists and non-physician endoscopists to perform screening colonoscopies to detect CRC at an early stage [33]. Our population may be more amenable to screening for CRC given the high percentage of rectal and left sided colon cancers being detected in Uganda.

#### **2.5 Limitations in Screening for CRC in Uganda and Other Low Income Countries in Sub-Saharan Africa**

In Europe and the USA observational studies and randomized controlled trials have shown a 30-year decline in the mortality and incidence of CRC [34,35].

A limiting factors for our ability to screen for CRC in Uganda is that pathological results may take as long as 6 weeks to process as they may need to be processed at other institutions. In future, high resolution micro-endoscopy may be used to detect colorectal malignancy in a timely manner [36].

Low income countries should consider the faecal occult blood test which has been most commonly used for screening CRC globally. Only 5-12% of patients with a positive faecal occult blood test will require a colonoscopy. Flexible sigmoidoscopy may also be more cost effective in our setting. Whilst these strategies have been implemented in other low income countries, in Sub-Saharan Africa their cost and feasibility still need evaluation.

In Sub-Saharan Africa, the current colonoscopy capacity is low and any increase in availability will need a parallel development in surgical and oncology infrastructure, pathology services and training physicians, surgeons and non-physician health workers including nurses in endoscopy. When considering and implementing screening in countries like Uganda, in order to meet National goals, additional support may be required from equipment suppliers and international Surgical and Medical societies.

### 3. CONCLUSIONS

An improvement in diagnosing, screening and treating CRC by increasing surgical and endoscopic capacity should be a public health priority in Uganda given the observed epidemiological shifts. However, in most of Sub-Saharan Africa, colorectal cancer screening is not yet a public health priority. When looking at CRC mortality the current discrepancy between CRC incidence between low income countries and high income countries greatly diminishes. Therefore in Uganda, in order to reduce this mortality there is need to expand the surgical, endoscopy and oncological infrastructure to care for CRC patients. Future implementation of National screening programmes to detect CRC at an early stage is also necessary to reduce the mortality.

Future collaborations and support from high income countries for endoscopic equipment and international medical and surgical societies from high income countries will help low income countries like Uganda in Sub-Saharan Africa to reach the goal of improving the access to care of colorectal carcinoma patients.

Determining the true burden from CRC in Uganda poses a challenge however the incidence of colorectal cancer is increasing in our hospitals which is consistent with findings from

other Sub-Saharan countries. These findings have implications not only for our hospitals in Uganda but also for Sub-Saharan Africa and the wider global community.

### CONSENT AND ETHICAL APPROVAL

Research and Ethical approval for this preliminary PhD work was obtained from the Doctoral committee and Higher Degrees Research and Ethics Committee of the School of Biomedical Sciences, College of Health Sciences, Makerere University. A waiver of consent was obtained from the Higher Degrees Research and Ethics Committee of the School of Biomedical Sciences, College of Health Sciences, Makerere University to use data from the Kampala Cancer Registry. Informed consent/assent was obtained from prospectively recruited participants taking into consideration the principles of good clinical practice. Uganda National Council for Science and Technology gave final approval for this project.

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### COMPETING INTERESTS

Author has declared that no competing interests exist.

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