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Pediatric Colorectal Cancer in Africa: A Multicenter Study on Epidemiology, Management, and Outcomes Between 2000 and 2023

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Abbreviations: 5-FU, 5-fluorouracil; CAPEOX, capecitabine, oxaliplatin; CRC, colorectal cancer; CT, computed tomography; EFS, event-free survival; FAP, familial adenomatous polyposis; FOLFIRI, folinic acid, fluorouracil, irinotecan; FOLFOX, folinic acid, fluorouracil, oxaliplatin; HIC, high-income country; IQR, interquartile range; LMIC, low- and middle-income countries; MDT, multidisciplinary team; MRI, magnetic resonance imaging; NOS, not otherwise specified; OS, overall survival; PFS, progression-free survival; POUs, pediatric oncology units; SIOP, International Organization for Paediatric Oncology; SSA, Sub-Saharan Africa; XELOX, capecitabine, oxaliplatin.

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ABSTRACT

Introduction: Colorectal cancer (CRC) is increasing in Africa, yet reports in children and adolescents are limited. We describe the epidemiology, management, and survival outcomes of CRC in African children.

Methods: Retrospective data of children under 19 years diagnosed with CRC between 2000 and 2023 were collected from 14 African countries. Patient and tumor characteristics and treatment data were described and survival outcomes analyzed. GLOBOCAN data were used to evaluate age-related geographical distribution of CRC.

Results: Hundred-and-eight patients, 57.4% males, were diagnosed with a mean age of 14.9 (range 5–18) years. The mean symptom-onset-to-diagnosis duration was 90 days (range 2–1200). Most common symptoms were abdominal discomfort (70.6%) and change in bowel habits (57.8%). The commonest primary site was the ascending colon (30.6%) with a mean tumor size of 64.3 mm (range 30–150 mm) and 37% presenting in stage III and 36.1% in stage IV. Most (83.3%) tumors were confirmed on histology, of which 78.7% were adenocarcinoma. Carcinoembryonic antigen was performed in 38.9% of patients. Complete resection was achieved in 55.6% of cases, while 18.5% received radiotherapy. Folinic acid, Fluorouracil, Oxaliplatin (FOLFOX) was the first line chemotherapy in 48.1% of patients. A third of patients were lost to follow-up while 25.6% experienced disease progression. The 2-year and 5-year overall survival rates were 40.0% and 16.9%, respectively. Disease stage ($p = 0.07$) and degree of resection ($p = 0.02$) predicted outcomes.

Conclusion: Pediatric CRC is characterized by delayed diagnosis and advanced stage presentation, contributing to a significantly lower overall survival compared to adults. Focused research and multidisciplinary management are needed to understand pediatric CRC and improve outcomes.

1 | Introduction

Colorectal cancer (CRC) is mainly diagnosed in adults but is rare in children [1]. Pediatric CRC accounts for less than 1% of global childhood cancers [1, 2] due to the prolonged latency to malignant transformation period for CRC [3]. The main histological subtypes of CRC in children include adenocarcinoma, predominantly mucinous adenocarcinoma of up to 50%, and signet ring cell type, compared to 15% in adults [2]. Other histological types include neuroendocrine tumors and rare histology types distinct from adenocarcinoma [3].

The incidence of pediatric CRC varies globally and in high-income countries (HIC) less than five cases per million children per year have been reported [1, 2]. In contrast, in regions with limited resources and a higher burden of gastrointestinal diseases, underreporting of pediatric CRC may occur [1, 2]. In sub-Saharan Africa (SSA), CRC though relatively rare is rising due to urbanization and changing lifestyles [4]. While CRC is often associated with older adults, in SSA 19 to 38% of diagnoses occur in individuals under 40 years of age, but CRC in children and adolescents is not well documented [4]. In HIC, CRC in children contributes to 7% of cases [2]. It is postulated that the differences in resource limited settings are due to genetic predispositions, environmental exposures, and delayed detection [4]. CRC in African children may arise more frequently from benign polyps in the context of genetic syndromes like familial adenomatous polyposis (FAP), Lynch syndrome, syndromes with p53 mutations, and MUTYH-associated polyposis than sporadic cases [4, 5].

Adult CRC is linked to lifestyle factors like low-fiber or high-fat diets, alcohol consumption, and insulin resistance [6]. In children, inflammatory bowel disease and juvenile polyposis significantly increase risk, while poor diet and obesity are emerging concerns [2, 6, 7]. Asia, particularly India and Japan, shows rising early-onset CRC due to distinct genetic and environmental interactions [2, 6, 7]. Africa faces unique hurdles, including limited infrastructure, diagnostic tools, and a high burden of infectious diseases that confound CRC detection [8]. While underreported due to insufficient cancer registries, limited data suggest CRC may be more prevalent in Africa than once believed, especially where hereditary syndromes and pro-inflammatory diets are common [1, 2, 8].

Common CRC symptoms include persistent abdominal pain, altered bowel habits changing between diarrhea and constipation, rectal bleeding, and unintended weight loss [7, 9]. Due to the similarity of symptoms with other common pediatric gastrointestinal conditions, especially in Africa with high infectious gastro-intestinal disease burdens, diagnosis is often delayed [7, 9, 10]. The rarity of the diagnosis also contributes to misdiagnosis. The diagnosis is made utilizing a combination of abdominal imaging, from abdominal ultrasound scan to magnetic resonance imaging, whilst colonoscopy allows for visualization of polyps or tumors and performing a biopsy for pathological confirmation. Additional molecular testing is important to detect syndrome-associated mutations [7, 9].

The treatment of colorectal cancer in children involves a multidisciplinary approach, combining surgery, chemotherapy, and radiation therapy [11, 12]. The aim is to gain a complete resection, but the extent of surgery depends on the tumor's location and stage. Minimally invasive techniques, where feasible, are preferred to reduce recovery times. Adjuvant chemotherapy is used to target microscopic disease and reduce recurrence [11, 12]. Standard regimens include regimens with a fluorouracil (5-FU), oxaliplatin, and irinotecan backbone [11, 12]. Radiotherapy is rarely indicated in pediatric cases but may be necessary for rectal tumors or advanced tumors [11, 12]. Targeted therapies bevacizumab (anti-VEGF) and cetuximab (anti-EGFR) are indicated in tumors with the respective molecular characteristics [11, 12].

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The prognosis for children diagnosed with CRC is dependent on the stage at diagnosis and genetic factors [1, 2, 12]. Localized disease with complete surgical resection has a favorable outcome with a 5-year overall survival (OS) rate exceeding 80% [1, 2, 12]. Advanced stage disease with lymph node involvement or metastasis has a poorer prognosis, with 5-year survival rates as low as 20% [1, 2, 12]. Children with syndromes such as FAP have a markedly increased risk of recurrence or secondary malignancies and poor outcomes. In sub-Saharan Africa (SSA), colorectal cancer (CRC) management is severely constrained by limited access to colonoscopy, delayed pathology services, restricted surgical capacity, inadequate chemotherapy availability, and frequent presentation with advanced, incurable disease [1, 2, 12]. Consequently, only a small minority of pediatric patients receive care consistent with international standards, and treatment is often modified or unavailable. The absence of specialized pediatric oncology expertise further compromises management, which is frequently directed by adult providers. Fewer than 5% of patients receive standard CRC-directed therapy, and survival declines substantially without it [1, 2, 12]. The estimated 3-year overall survival in SSA, largely reflecting adult cohorts, is approximately 45%, while outcomes for children remain undefined [1, 2, 12]. Therefore, the aim of the study was to determine the basic epidemiology, clinical characteristics, management and survival outcomes of CRC in African children to highlight the management limitations in SSA to improve CRC outcomes in children and adolescents.

2 | Materials and Methods

To evaluate the pattern of distribution between adult and pediatric CRC, data on continental incidences were sourced from the International Agency for Research and Cancer's Global Cancer Observatory, GLOBOCAN [13] and converted to tables and figures.

Patient and tumor characteristics and survival data were sourced through SIOP Africa communication channels, SIOP Connect, and the SIOP Africa WhatsApp group. SIOP Africa has 530 members representing 41 African countries; all POUs in Africa with their associated pathology and adult oncology departments were invited to participate in a study investigating patient and tumor characteristics and treatment outcomes. Data of all children under 19 years diagnosed with CRC confirmed on pathology from 2000 to 2023 were requested for inclusion. Data were captured electronically and analyzed using IBM SPSS Version 25 (IBM Corporation, USA) statistical software. Frequencies, means, medians, and ranges were described. Differences in medians and means were assessed using the Mann–Whitney *U* test or Student's *t*-test. Fisher's exact test was applied in cohorts of fewer than five observations. For the evaluation of survival and variate analyses, only patients diagnosed with adenocarcinoma were excluded to ensure a homogenous histological subtype. For the evaluation of EFS, there were events data available for 93 patients, and for OS survival outcome data for 87 patients. Lost to follow-up was defined as patients who did not attend appointments for 6 months or more despite attempts to contact them. To evaluate a possible cohort contribution bias by the Egyptian cohort, survival analyses were additionally done in an Egyptian cohort and a Non-Egyptian cohort. A substantial proportion of patients were lost to follow-up, particularly in the non-Egyptian cohort. As Kaplan–Meier and Cox regression methods assume non-informative censoring, this may introduce bias if patients lost to follow-up differ systematically from those retained. Given the substantial proportion of patients lost to follow-up, sensitivity analyses were performed using alternative assumptions. In the primary analysis, patients lost to follow-up were censored at last contact. In a best-case scenario, all patients lost to follow-up were assumed alive at 31 December 2024, whereas in a worst-case scenario they were assumed deceased at their last documented follow-up. For all calculations, a p-value less than 0.05 was considered significant. The study was reported using the STROBE guidelines for cross sectional studies.

The Antwerp University Hospital Research Ethics Committee (Project ID 7440) granted ethical approval. Where necessary, approval was obtained from local ethics committees.

3 | Results

3.1 | African Continental Incidences of Colorectal Cancer

According to GLOBOCAN 2022 data, there are distinct differences in the distribution of age-standardized incidence rates between pediatric and adult populations [13]. The highest ASIR per 100000 children in the African pediatric population (Figure 1A) was in Sudan (0.54), Eritrea (0.42), Central African Republic (0.32), Chad (0.27), Libya (0.27), Angola (0.18) and Egypt (0.17), thus predominantly central and north-east Africa. In contrast, the highest ASIR per 100000 adults (Figure 1B) were in Zimbabwe (207.9), South Africa (203.4), Reunion (203.1), Namibia (193.48), Egypt (166.1), Zambia (159.5), Malawi (159.5) and Uganda (154.3), which are predominantly in Southern and East Africa.

3.2 | Demographic Distribution of Pediatric CRC Patients

One-hundred and eight children were included in the study from 14 (25.9%) African countries (Figure 2, Table 1). The largest contribution was from Egypt ($n = 43$; 39.8%), followed by Tunisia ($n = 13$; 12.0%), Nigeria and Angola with 12 patients (11.1%) each. Sixty (55.6%) were from North Africa, 19 (17.6%) from Southern Africa, 16 (14.8%) from West Africa and 13 (12.0%) from East Africa. The majority ($n = 95$; 88.0%) were from a lower-middle-income country, eight (7.4%) from a low-income country and only five (4.6%) were from an upper-middle-income country (Table 1).

3.3 | Patient and Tumor Characteristics

Collectively, there was a male predominance (57.4%) with a 1:0.7 ratio. Kenya, Zimbabwe and Uganda had a female predominance (Table 2). The median age at diagnosis was 14.9 years (IQR ±3.1 years) with a range between 5 and 18 years (Table 2). In the entire cohort, the median duration of symptoms before diagnosis was 90 days (IQR ±135 days) with a range between

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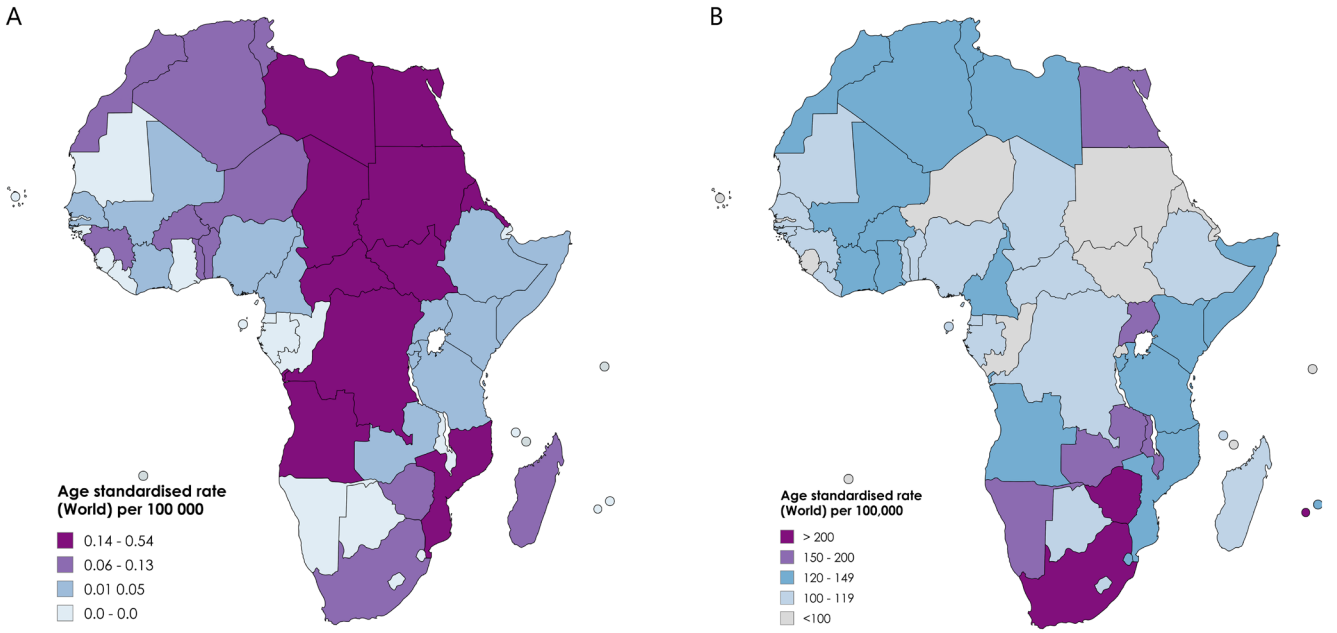


FIGURE 1 | (A) The age-standardized incidence rate distribution of pediatric CRC in Africa. (B) The age-standardized incidence rate distribution of adult CRC in Africa.

2 and 1200 days. The most common symptom was abdominal discomfort ($n = 79$; 73.1%) followed by a change in bowel habits ($n = 63$; 58.3%), weight loss ($n = 49$; 45.4%) and blood in the stool ($n = 48$; 44.4%).

The three most common primary sites were the ascending colon ($n = 33$; 30.6%), rectum ($n = 28$; 25.9%), and the descending colon ($n = 18$; 16.7%) (Table 2). Synchronous tumors in two sites were present in 10 (9.3%) children. The median tumor diameter for all patients was 60 mm (IQR ±35 mm) with a range between 30 and 150 mm. Distant metastatic disease was present in 36.1% ($n = 39$) of the cohort, with the highest number of patients ($n = 40$; 37.0%) presenting with Stage 3 (Table 2).

A biopsy was performed to confirm the diagnosis in 90 patients (83.3%) (Table 3), a pathology confirmation was obtained by primary resection in 5 (4.6%) and a radiological diagnosis without being biopsied was made in 13 (12%) patients. Of these, the pathology was confirmed by tumor resection in 11 (1.0%) patients. Of the 106 (98.1%) histological diagnoses, the most common histological type for those tumors that were biopsied was adenocarcinoma ($n = 95$; 88.0%) (Table 2), followed by carcinoma NOS ($n = 7$; 6.5%). Of the adenocarcinoma cohort, the subtypes included 38 (40.0%) mucinous, 6 (6.3%) signet-ring cell, and 51 (53.7%) unknown histological subtypes. There were three (2.8%) neuro-endocrine tumors. Carcinoembryonic antigen (CEA) assay was positive in 32 (29.6%) patients, but was not done in 66 (61.1%) patients. The median CEA tumor marker value was 13.3 ng/L (IQR ±86 ng/L) with a range between 0.1 and 1000 ng/L (Table 2). The median size of the tumors was 60 mm (IQR ±35) and a range of 3–150 mm (Table 2). Molecular tests were not done on any tumor.

A family history of CRC was reported in 2 (1.9%) patients (twin females). Three CRC associated syndromes related to MLH1, MSH2, MSH6, or PMS2 genes were evaluated. Syndromes were documented in only 16 (14.8%) patients: 12 (75.0%) with Familial polyposis, 3 (18.8%) with Lynch syndrome and one (6%) with Constitutional mismatch repair deficiency (CMMRD) syndrome. This may be a false low value since predisposing factors were not documented in all patients (Table 2).

3.4 | Management of Pediatric Colorectal Cancers in Africa

Most patients ($n = 75$; 69.4%) were co-managed with adult oncology services. Complete and incomplete resections were achieved in 55.% and 18.5% respectively (Table 3), and no interventions or biopsy only were documented in 25.9% ($n = 28$) of patients. The first-line chemotherapy regimens varied considerably: Folinic acid, Fluorouracil, Oxaliplatin (FOLFOX) was administered in 48.1% ($n = 52$) of patients, followed by a Capecitabine-oxaliplatin combination (XELOX or CAPEOX)($n = 13$; 12.1%), Capecitabine (Xeloda) ($n = 8$; 7.4%) and 5-FU in five *p* (4.6%) patients. The majority of patients ($n = 85$; 78.7%) did not receive radiotherapy and was not reported in 2 (Table 3). Targeted therapies were only administered in 11 (10.2%) patients. Only one (< 1%) patient received a targeted therapy, Cetuximab, during first line chemotherapy. The remaining 10 (9.3%) patients received targeted therapies during second line chemotherapy. Of these seven received Bevacizumab, two received Cetuximab and one received Pembrolizumab.

3.5 | Survival Events and Outcomes

Nearly all patients ($n = 95$; 87.9%) experienced survival-determining events (Table 3). Of all events, lost-to-follow-up

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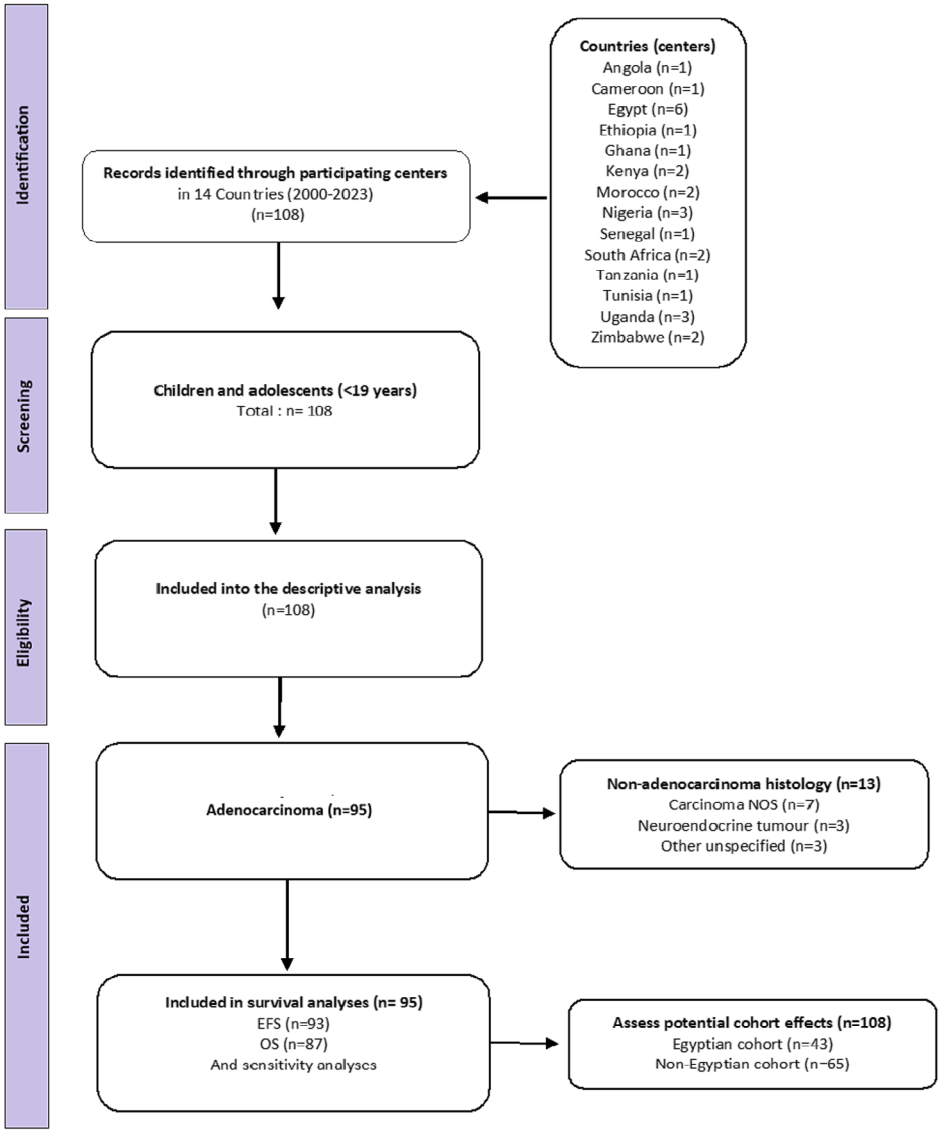


FIGURE 2 | Flowchart for cohort selection.

was the most common ($n=34$: 35.8%) followed by tumor progression ($n=24$; 25.6%) and death ($n=21$; 22.1%). At the end of the study period, 43 (39.8%) patients died, and 18 (16.7%) were lost to follow-up. The median follow-up period was 14.1 months (IQR ±21.3 months) with a range of 1 to 247.6 months.

The 2-year and 5-year event-free survival (EFS) (Table 1) were 29.9% (95% CI 20.2%–39.5%) and 11.4% (95% CI 3.8%–18.9%), respectively. Although insignificant, the highest 2-year and 5-year EFS, excluding Ghana with a single patient, were reported from Tunisia with 63.6% (35.2%–92.1%) and 27.3% (1.0%–53.6%), respectively ($p=0.56$). Stage 4 disease had the poorest 2-year [19.4% (5.5%–33.4%)] and 5-year EFS [9.7% (0.0%–20.2%)] ($p=0.05$). Achieving a complete resection had the best 2-year [38.7% (25.4%–51.9%)] and 5-year EFS [17.4% (6.2%–28.5%)] ($p=0.01$). The region, sex, primary site, CEA assay, and radiotherapy didn't show a statistically significant EFS.

The 2-year and 5-year OS for the entire sample (Table 1) were 40.0% (95% CI: 29.3%–50.8%) and 16.9% (95% CI: 7.4%–26.3%), respectively ($p<0.001$). Tunisia had the highest 2-year and 5-year OS with 72.7% (46.4%–99.0%) and 45.5% (16.0%–74.9%), respectively ($p=0.59$). Stage 4 disease had the poorest 2-year [23.4% (8.3%–38.6%)] and 5-year OS [10.0% (0.0%–20.8%)] ($p=0.02$) (Figure 3). Achieving a complete resection had the best 2-year [56.0% (41.7%–70.3%)] and 5-year OS [17.4% (28.6% (13.8%–43.5%))] ($p<0.01$) (Figure 4). The region, sex, primary site, CEA assay and radiotherapy didn't show a statistically significant OS.

3.6 | Sensitivity Analysis for Loss to Follow-Up

For the overall cohort, 5-year overall survival ranged from 16.6% (worst-case) to 58.4% (best-case), compared with 39.2% in the primary analysis (Table S1). Similar patterns were observed in the Egypt cohort (11.7%–46.2%) and non-Egypt cohort (19.1%–67.6%). Importantly, the non-Egypt cohort consistently demonstrated superior survival compared with the Egypt cohort across all scenarios, suggesting that the direction of the observed findings was robust despite uncertainty introduced by loss to follow-up.

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TABLE 1 | Demographic distribution of patients with patient, tumor and treatment related outcomes of children diagnosed with CRC in Africa.

		N = 93 patients with events data			*N* = 87 patients with date of death data		
Factor	***N* (%)**	**2-year EFS (95% CI)**	**5-year EFS (95% CI)**	***p***	**2-year OS (95% CI)**	**5-year OS (95% CI)**	***p***
Country							
Total	108 (100)	29.9% (20.2%–39.5%)	11.4% (3.8%–18.9%)	0.01	40.0% (29.3% – 50.8%)	16.9% (7.4% – 26.3%)	< 0.01
Egypt	43 (39.8)	27.3% (12.4%–42.1%)	11.7% (0.0%–25.3%)	0.56	37.2% (21.1%–53.3%)	11.6% (0.0%–25.6%)	0.59
Tunisia	13 (12.0)	63.6% (35.2%–92.1%)	27.3% (1.0%–53.6%)		72.7% (46.4%–99.0%)	45.5% (16.0%–74.9%)	
Angola	12 (11.1)	18.2% (0.0%–41.0%)	0.0% (0.0%–0.0%)		20.0% (0.0%–55.1%)	0.0% (0.0%–0.0%)	
Nigeria	12 (11.1)	22.2% (0.0%–49.4%)	0.0% (0.0%–0.0%)		22.2% (0.0%–49.4%)	0.0% (0.0%–0.0%)	
South Africa	5 (4.6)	60.0% (17.1%–100%)	30.0% (0.0%–76.8%)		60.0% (17.1%–100%)	30.0% (0.0%–76.8%)	
Uganda	5 (4.6)	0.0% (0.0%–0.0%)	0.0% (0.0%–0.0%)		0.0% (0.0%–0.0%)	0.0% (0.0%–0.0%)	
Kenya	4 (3.7)	50.0% (1.0%–99.0%)	50.0% (1.0%–99.0%)		37.5% (0.0%–93.6%)	37.5% (0.0%–93.6%)	
Morocco	4 (3.7)	0.0% (0.0%–0.0%)	0.0% (0.0%–0.0%)		25.0% (0.0%–67.4%)	0.0% (0.0%–0.0%)	
Ethiopia	3 (2.8)	33.3% (0.0%–86.7%)	0.0% (0.0%–0.0%)		100.0% (100%–100%)	0.0% (0.0%–0.0%)	
Zimbabwe	2 (1.9)	0.0% (0.0%–0.0%)	0.0% (0.0%–0.0%)		0.0% (0.0%–0.0%)	0.0% (0.0%–0.0%)	
Ghana	1 (0.9)	100.0% (100%–100%)	100.0% (100%–100%)		100.0% (100%–100%)	100.0% (100%–100%)	
Senegal	1 (0.9)	0.0% (0.0%–0.0%)	0.0% (0.0%–0.0%)		0.0% (0.0%–0.0%)	0.0% (0.0%–0.0%)	
Tanzania	1 (0.9)	0.0% (0.0%–0.0%)	0.0% (0.0%–0.0%)		0.0% (0.0%–0.0%)	0.0% (0.0%–0.0%)	
Cameroon	1 (0.9)	0.0% (0.0%–0.0%)	0.0% (0.0%–0.0%)		0.0% (0.0%–0.0%)	0.0% (0.0%–0.0%)	
Region							
North Africa	60 (55.6)	33.3% (20.3%–46.3%)	14.3% (3.4%–25.2%)	0.15	44.3% (30.8%–57.9%)	20.2% (7.7%–32.6%)	0.117
Southern	19 (17.6)	27.8% (7.1%–48.5%)	6.9% (0.0%–19.8%)		33.3% (6.7%–60.0%)	11.1% (0.0%–31.0%)	
West Africa	16 (14.8)	18.3% (0.0%–41.3%)	0.0% (0.0%–0.0%)		20.5% (0.0%–45.7%)	0.0% (0.0%–0.0%)	
East Africa	13 (12.0)	27.8% (0.0%–59.5%)	13.9% (0.0%–38.8%)		45.0% (8.1%–81.9%)	22.5% (0.0%–58.7%)	
World Bank Income Group							
LIC	8 (7.4)	20.0% (0.0%–55.1%)	0.0% (0.0%–0.0%)	0.621	50.0% (1.0%–99.0%)	0.0% (0.0%–0.0%)	0.577
LMIC	95 (88.0)	28.8% (18.7%–38.9%)	11.1% (3.2%–19.1%)		38.2% (26.9%–49.6%)	16.6% (6.8%–26.5%)	
UMIC	5 (4.6)	60.0% (17.1%–100%)	30.0% (0.0%–76.8%)		60.0% (17.1%–100%)	30.0% (0.0%–76.8%)	
Sex							
Male	62 (57.4)	31.8% (18.7%–44.9%)	8.5% (0.0%–17.4%)	0.71	41.3% (26.8%–55.7%)	13.3% (1.7%–24.8%)	0.584
Female	46 (42.6)	27.5% (13.4%–41.6%)	15.7% (2.8%–28.7%)		38.4% (22.3%–54.5%)	21.6% (6.2%–37.0%)	
Primary site							
Ascending colon	33 (30.6)	27.8% (10.9%–44.6%)	4.8% (0.0%–13.7%)	0.996	47.6% (28.6%–66.6%)	18.8% (0.9%–36.6%)	0.916
Rectum	28 (25.9)	26.2% (7.3%–45.2%)	17.5% (0.0%–36.3%)		28.1% (6.7%–49.5%)	18.7% (0.0%–39.4%)	
Descending colon	18 (16.7)	33.8% (9.0%–58.5%)	16.9% (0.0%–43.3%)		34.3% (9.5%–59.1%)	17.1% (0.0%–43.9%)	
Other	29 (26.9)	33.3% (14.8%–51.8%)	12.5% (0.0%–25.7%)		44.6% (23.5%–65.7%)	14.9% (0.0%–30.3%)	

(Continues)

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TABLE 1 | (Continued)

Factor	*N* (%)	*N* = 93 patients with events data		*p*	*N* = 87 patients with date of death data		*p*
		2-year EFS (95% CI)	5-year EFS (95% CI)		2-year OS (95% CI)	5-year OS (95% CI)	
Stage							
Stage 0	2 (1.9)	100% (100%–100%)	0.0% (0.0%–0.0%)	0.05	100% (100.0%–100%)	0.0% (0.0%–0.0%)	0.02
Stage 1	1 (0.9)	0.0% (0.0%–0.0%)	0.0% (0.0%–0.0%)		100% (100%–100%)	100.0% (100%–100%)	
Stage 2	20 (18.5)	28.6% (8.2%–48.9%)	19.0% (0.0%–39.5%)		51.4% (27.3%–75.5%)	25.7% (1.9%–49.6%)	
Stage 3	40 (37.0)	42.4% (25.2%–59.5%)	14.8% (0.2%–29.4%)		46.1% (28.4%–63.9%)	21.1% (4.0%–38.3%)	
Stage 4	39 (36.1)	19.4% (5.5%–33.4%)	9.7% (0.0%–20.2%)		23.4% (8.3%–38.6%)	10.0% (0.0%–20.8%)	
Unknown	6 (5.6)	20.0% (0.0%–55.1%)	0.0% (0.0%–0.0%)		0.0% (0.0%–0.0%)	0.0% (0.0%–0.0%)	
Tumor marker (CEA assay)							
Positive	32 (29.6)	25.8% (7.8%–43.8%)	6.9% (0.0%–19.3%)	0.56	38.5% (18.3%–58.7%)	16.5% (0.0%–35.5%)	0.771
Negative	10 (9.3)	40.0% (9.6%–70.4%)	26.7% (0.0%–56.1%)		48.0% (15.9%–80.1%)	32.0% (0.0%–65.4%)	
Unknown	66 (61.1)	30.6% (18.2%–43.0%)	10.4% (1.1%–19.6%)		40.4% (26.5%–54.3%)	14.8% (3.4%–26.2%)	
Surgery							
Complete resection	60 (55.6)	38.7% (25.4%–51.9%)	17.4% (6.2%–28.5%)	0.01	56.0% (41.7%–70.3%)	28.6% (13.8%–43.5%)	<0.001
Incomplete resection	20 (18.5)	23.5% (3.4%–43.7%)	0.0% (0.0%–0.0%)		28.2% (6.2%–50.2%)	0.0% (0.0%–0.0%)	
Biopsy only	18 (16.7)	20.5% (0.0%–45.7%)	0.0% (0.0%–0.0%)		20.5% (0.0%–45.7%)	0.0% (0.0%–0.0%)	
No surgery	10 (9.2)	0.0% (0.0%–0.0%)	0.0% (0.0%–0.0%)		0.0% (0.0%–0.0%)	0.0% (0.0%–0.0%)	
Radiotherapy							
Not irradiated	85 (78.7)	30.6% (19.7%–41.5%)	11.8% (3.3%–20.3%)	0.07	41.2% (29.1%–53.2%)	18.9% (7.9%–29.9%)	0.038
Irradiated	20 (18.5)	30.9% (8.8%–53.0%)	10.3% (0.0%–28.3%)		40.1% (14.7%–65.5%)	10.0% (0.0%–28.2%)	
Unknown	2 (1.8)	0.0% (0.0%–0.0%)	0.0% (0.0%–0.0%)		0.0% (0.0%–0.0%)	0.0% (0.0%–0.0%)	

Abbreviations: CI, confidence interval; EFS, event free survival; LIC, low-income country; LMIC, lower-middle income country; OS, overall survival; UMIC, upper-middle income country.

3.7 | Variate Analysis

On univariate analysis, only metastatic disease (Stage 4) ($p = 0.07$) and gaining a complete resection ($p = 0.02$) were possible predictors of outcome. On multivariate analysis, only a complete resection ($p = 0.04$) remained a significant factor (Table 4).

4 | Discussion

This contemporary overview of pediatric CRC reported from Africa highlights epidemiological, clinical, and outcome disparities when compared with adult populations in Africa. CRC in children and adolescents under 19 years in Africa is rare but increasing [13]. Using population-level incidence data alongside a multinational clinical cohort, this study demonstrates that pediatric CRC in Africa remains geographically heterogeneous, with higher pediatric incidence rates concentrated in North and Central–East Africa, contrasting sharply with adult disease patterns [14]. Children in this cohort presented predominantly in adolescence, after prolonged symptom duration and with advanced disease. Management strategies varied widely, reflecting differences in resource availability and reliance on adult oncology services, with limited access to radiotherapy and inconsistent use of stool-based screening or serum tumor markers. Survival outcomes were poor, with low EFS and OS compared with global benchmarks, driven largely by advanced stage at presentation, incomplete surgical resection, and high rates of loss to follow-up.

Most children presented with multiple, non-specific gastrointestinal symptoms, especially abdominal discomfort and changes in bowel habits. Classic warning signs and symptoms such as bleeding or weight loss were common but not generalizable to the whole cohort. Overall, the symptom profile was heterogeneous and often non-specific, contributing to possible delays in recognition and late-stage diagnoses. Compared with adults, the symptom profile is comparable but in adults typical warning signs and symptoms are more common in clinical thinking and differential diagnoses [15, 16]. In children the same symptoms are often attributed to benign causes, including infections, autoimmune diseases and metabolic disorders [15, 17]. Typical

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TABLE 2 | Patient and tumor related characteristics of children diagnosed with CRC in Africa.

Factor	*N* (%)		
Patient characteristics			
Sex $n = 108$			
Female	46 (42.6)		
Male	62 (57.4)		
Total and M:F ratio	108 (100) ratio 1:0.7		
Age at diagnosis $n = 108$			
Mean (range)	14.9 years (5.0–18.0)		
Median (IQR)	15.0 years (±4.0)		
0–5 years	1 (0.9)		
6–10 years	9 (8.3)		
> 10 years	98 (90.8)		
Tumor characteristics			
Duration of symptoms $n = 101$			
Mean (range)	165.2 days (2–1200)		
Median (IQR)	90 days (±135)		
Symptoms	**Yes**	**No**	**Unknown**
Blood in the stool	48 (44.4)	52 (48.1)	8 (7.4)
Change in bowel habits	63 (58.3)	41 (38.0)	4 (3.7)
General abdominal discomfort	79 (73.1)	24 (22.2)	5 (4.6)
Unintended weight loss	49 (45.4)	50 (46.3)	9 (8.3)
Fatigue	34 (31.5)	61 (56.5)	13 (12.0)
Vomiting	41 (38.0)	59 (54.6)	8 (7.4)
Other symptoms		***N* (%)**	
Intestinal obstruction		5 (4.6)	
Abdominal swelling/ distention		5 (4.6)	
Lower back pain		3 (2.8)	
Primary tumor site $n = 108$			
Ascending colon		33 (30.6)	
Rectum		28 (25.9)	
Descending colon		18 (16.7)	
Synchronous in two sites		10 (9.3)	
Transverse colon		7 (6.5)	
Recto-sigmoid		7 (6.5)	
Not documented or unknown		(4.6)	

(Continues)

TABLE 2 | (Continued)

Factor	*N* (%)
Tumor size (longest diameter) $n = 92$	
Mean (range)	64.3 mm (30–150)
Median (IQR)	60.0 mm (±35)
Stage $n = 108$	
Stage 0	2 (1.9)
Stage 1	1 (0.9)
Stage 2	20 (18.5)
Stage 3	40 (37.0)
Stage 4	39 (36.1)
Unknown	6 (5.6)
Carcinoembryonic antigen (CEA) value at diagnosis $n = 38$	
Mean (range)	110.52 (0.1–1000)
Median (IQR)	13.25 (±86.02)
Histological categories	
Adenocarcinoma	95 (88.0)
Mucinous	38/95 (40.0)
Signet ring cell	6/95 (6.3)
Not subtyped or unknown	51/95 (53.7)
Undifferentiated carcinoma	1 (0.9)
Carcinoma NOS	7 (6.5)
Unknown or other	5 (4.6)
Neuro-endocrine tumors	3 (2.8)
Histological grading	
Adenocarcinoma	95 (88.0)
Well-differentiated (Grade I)	6/95 (6.3)
Moderately differentiated (Grade II)	12/95 (12.6)
Poorly differentiated (Grade III)	9/95 (9.5)
Ungraded	68/95 (71.6)
Associated syndromes	
Familial adenomatous polyposis	12 (11.1)
Lynch syndrome	3 (2.8)
CMMRD	1 (0.9)
Unknown or undocumented	92 (85.2)
Total	108 (100)

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TABLE 3 | Treatment related factors of children diagnosed with CRC in Africa.

Treatment modalities	
Treatment factors	***N* (%)**
Diagnostic modalities	
Histology	106 (98.1)
Initial biopsy	90 (83.3)
Primary resection	16 (14.8%)
Radiological imaging (CT/MRI)	13 (12.1)
Scope (colonoscopy)	4 (3.7)
Digital rectal examination	1 (0.9)
Surgery	
Complete resection	60 (55.6)
Incomplete resection	20 (18.5)
Biopsy only	18 (16.7)
No surgery	10 (9.2)
Radiotherapy	
Not irradiated	85 (78.7)
Irradiated	20 (18.5)
Unknown	2 (1.8)
Chemotherapy (first line)	
FOLFOX	52 (48.1)
Capecitabine (Xeloda)	8 (7.4)
Capecitabine-oxaliplatin combination	13 (12.1)
XELOX	7 (6.5)
CAPEOX	6 (5.6)
5-FU	5 (4.6)
FOLFIRI	4 (3.7)
Other	9 (8.3)
None	18 (16.7)
Chemotherapy (second line)	
FOLFIRI	9 (8.3)
FOLFIRI combined with immunotherapy	7 (6.5)
Bevacizumab	5 (4.6)
Cetuximab	2 (1.8)
Other	11 (10.2)
None	81 (75.0)
Targeted therapies	
Total	12 (11.1)
Bevacizumab (second line)	8 (7.4)
Cetuximab (1× first line and 2× second line)	3 (2.8)
Pembrolizumab (second line)	1 (0.9)
None administered	93 (86.1)
Unknown	3 (2.8)
Collaboration with adult oncology services	
Yes	76 (70.3)
No	30 (27.8)
Unknown	1 (0.9)
Events during treatment	
Lost to follow up	34 (31.4)
Progression	24 (22.2)
Death	21 (19.4)
No event	13 (12.0)
Relapse	12 (11.1)
Secondary malignancy	4 (3.7)
Follow up period	
Mean (range)	24.6 months (0.0–247.6)
Median (IQR)	14.1 months (21.3)

Abbreviations: 5-FU, 5-fluorouracil; CAPEOX, capecitabine, oxaliplatin; CT, computed tomography; FOLFIRI, folinic acid, fluorouracil, irinotecan; FOLFOX, folinic acid, fluorouracil, oxaliplatin; IQR, interquartile range; MRI, magnetic resonance imaging; XELOX, capecitabine, oxaliplatin.

adult-type malignancies are considered much lower in pediatric differential diagnoses and mostly misdiagnosed [15, 17].

In the pediatric cohort, tumors were more often right sided or in the ascending colon and rectum, with fewer in the sigmoid/rectosigmoid. In adults, colorectal cancer is usually distal-predominant arising in the sigmoid colon and rectum, with right-sided and proximal tumors increasing mainly in older populations [15, 17]. Tumor biology in children and adolescents was characterized by a predominance of adenocarcinoma, frequent mucinous and signet ring subtypes [2, 17, 18], and a notable proportion of underlying cancer predisposition syndromes. The high proportion of ungraded colorectal cancer histology in this study is likely due to limited pathology infrastructure, shortages of specialist gastrointestinal pathologists, reliance on small diagnostic biopsies rather than resection specimens, and incomplete pathology reporting in resource-constrained settings. In addition, histological grading requires assessment

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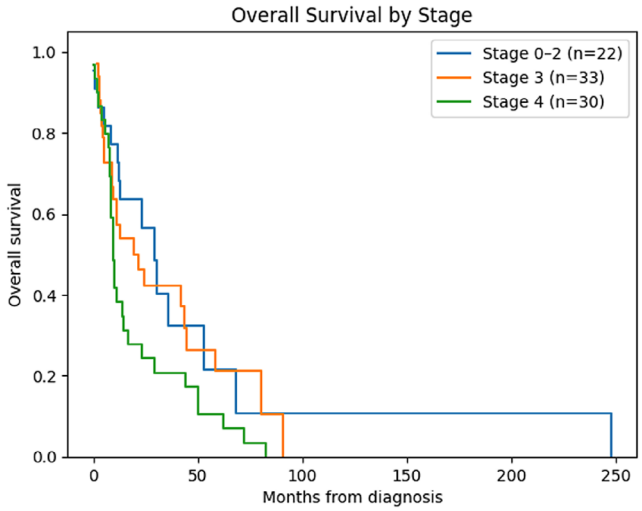


FIGURE 3 | Overall survival Kaplan-Meier curves by stage of children diagnosed with CRC in Africa.

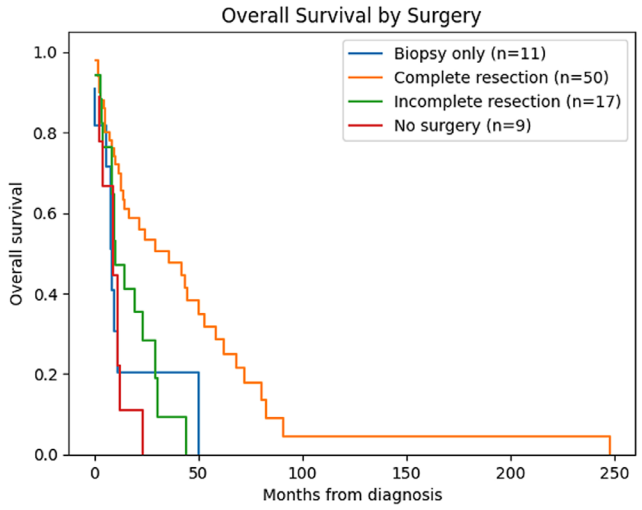


FIGURE 4 | Overall survival Kaplan-Meier curves by surgery of children diagnosed with CRC in Africa.

of tumor differentiation according to WHO criteria, which may not be feasible when tissue quality is poor, samples are limited, or pathology reports lack standardized reporting elements [19].

When contextualized against outcomes reported in adults and in pediatric cohorts from other regions, the survival observed in this African pediatric cohort is strikingly poor and highlights fundamental inequities in cancer care [2, 17, 18]. In adults, colorectal cancer outcomes in Africa are already inferior to those in high-income countries [17], though reported 5-year overall survival rates in adult African series commonly range between 30% and 60%, particularly where surgery and systemic therapy are accessible. By contrast, the 5-year overall survival of less than 20% observed in this pediatric cohort underscores an even greater vulnerability of children, despite their generally superior physiological resilience and treatment tolerance.

Compared with pediatric colorectal cancer outcomes from other countries, the disparity is comparable or more pronounced [20]. Published series from Europe and North America report 5-year overall survival rates up to 60% for children and adolescents, even though pediatric CRC is biologically aggressive and frequently associated with mucinous or signet ring histology [20]. In those settings, earlier diagnosis, routine access to high-quality pathology, timely complete surgical resection, standardized multimodal therapy, and structured long-term follow-up substantially mitigate the adverse prognostic impact of tumor biology. In contrast, children in the present African cohort, but also South America and Turkey, experienced prolonged diagnostic delays, advanced stage at presentation, inconsistent access to biopsy and tumor markers, limited radiotherapy use, and high rates of treatment interruption and loss to follow-up [20].

Notably, while advanced stage and metastatic disease predict poor outcomes across all age groups and regions, the dominant prognostic role of complete surgical resection in this study mirrors findings from both adult and pediatric international literature [21, 22]. However, the lower rate of complete resections achieved in this cohort reflects the complexity of resecting progressive tumors and surgical capacity constraints. Furthermore, the high prevalence of cancer predisposition syndromes, similar to 5%–15% of pediatric cohorts globally [23], suggests that outcomes could be substantially improved through earlier recognition and surveillance of at-risk children, an opportunity largely unrealized in many African settings. In children and adolescents, CEA has limited and inconsistent utility, because most pediatric intestinal tumors, even in pediatric colorectal adenocarcinoma, do not reliably elevate CEA [24]. This makes the diagnostic and prognostic value uncertain [24] even more in the pediatric population where CEA has not been studied extensively. While serial CEA monitoring may help in the small subgroup with CEA-producing tumors, a normal CEA offers little reassurance and limits its usefulness for surveillance in most pediatric patients [24, 25].

Overall, these comparisons indicate that the unfavorable outcomes observed are driven less by uniquely aggressive disease biology and more by systemic limitations in early detection, multidisciplinary management, and continuity of care. Closing the survival gap between African children, African adults, and children in high-income countries will therefore depend on strengthening health system capacity, improving referral pathways, and integrating pediatric-specific oncologic expertise into colorectal cancer care across the continent [26, 27]. Most importantly, this will depend on standardized management and access to chemotherapy and targeted therapies [26, 27] even in well-resourced settings [28]. Since the most effective targeted therapy treating CRC depends on the molecular profile of each tumor, increasing access to molecular and genetic diagnostics becomes more important in rare tumors, including pediatric CRC [29].

When evaluating the literature on the increased incidence of CRC in children, the causes remain unclear, but epigenetic mechanisms involving the parents, the child, or their interaction may contribute [29, 30]. Epigenetic alterations can arise from maternal stress, malnutrition or infections and may be transmitted across generations or occur directly in the child

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TABLE 4 | Variate analysis of patient, tumor and management related factors of children diagnosed with CRC in Africa.

Factor	*N* (%)	HR	95% CI		*p*
			Lower limit	Upper limit	
Univariate analysis					
Age					
≤ 10 years	10 (9.2)	Baseline			
> 10 years	98 (90.8)	1.24	0.44	3.51	0.68
Sex					
Female	46 (42.6)	Baseline			
Male	62 (57.4)	0.84	0.54	1.32	0.45
Stage					
Stage 0,1,2	23 (21.3)	Baseline			
Stage 3	40 (37.0)	1.15	0.61	2.17	0.67
Stage 4	39 (36.1)	1.76	0.95	3.25	0.07
Unknown	6 (5.6)	3.16	1.14	8.78	0.03
Primary site					
Rectum	33 (30.6)	Baseline			
Ascending colon	28 (25.9)	0.88	0.48	1.62	0.69
Descending colon	18 (16.7)	0.91	0.45	1.85	0.80
Other	29 (26.9)	0.86	0.47	1.58	0.63
Surgery					
Biopsy only	18 (16.7)	Baseline			
Complete resection	60 (55.6)	0.42	0.21	0.86	0.02
Incomplete resection	20 (18.5)	0.72	0.32	1.62	0.72
No surgery	10 (9.2)	1.22	0.49	3.02	0.67
Radiotherapy					
Not irradiated	85 (78.7)	Baseline			
Irradiated	20 (18.5)	0.95	1.16	20.6	0.87
Unknown	2 (1.8)	4.89	0.54	1.69	0.03
Multivariate analysis					
Age					
≤ 10 years	10 (9.2)	Baseline			
> 10 years	98 (90.8)	1.31	0.55	3.44	0.54
Sex					
Female	46 (42.6)	Baseline			
Male	62 (57.4)	1.11	0.65	1.89	0.69
Stage					
Stage 0,1,2	23 (21.3)	Baseline			
Stage 3	40 (37.0)	1.32	0.67	2.63	0.42
Stage 4	39 (36.1)	1.73	0.81	3.67	0.15
Unknown	6 (5.6)	5.52	1.63	18.75	0.006

(Continues)

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TABLE 4 | (Continued)

Factor	*N* (%)	HR	95% CI		*p*
			Lower limit	Upper limit	
Primary site					
Rectum	33 (30.6)	Baseline			
Ascending colon	28 (25.9)	0.57	0.22	1.49	0.25
Descending colon	18 (16.7)	0.69	0.32	1.46	0.33
Other	29 (26.9)	0.51	0.24	1.12	0.09
Surgery					
Biopsy only	18 (16.7)	Baseline			
Complete resection	60 (55.6)	0.40	0.16	0.97	0.04
Incomplete resection	20 (18.5)	0.94	0.37	2.37	0.90
No surgery	10 (9.2)	1.61	0.53	4.92	0.40
Radiotherapy					
Not irradiated	85 (78.7)	Baseline			
Irradiated	20 (18.5)	0.76	0.35	1.63	0.48
Unknown	2 (1.8)	3.31	0.57	19.05	0.18

Abbreviations: CI, confidence interval; HR, hazard ratio; LIC, Low-income country; LMIC, lower-middle-income country; UMIC, upper-middle-income country; WBIG, World Bank Income Group.

[29, 30]. The African countries with the highest pediatric CRC incidence share several factors that may influence epigenetic regulation, including malnutrition (folate, vitamin B12, iron and protein deficiencies), which can impair DNA methylation and gene regulation [31]. In addition, chronic exposure to infectious diseases such as malaria, tuberculosis, HIV and parasitic infections may alter DNA methylation and histone modification patterns, while environmental pollutants, including heavy metals, pesticides and microplastics, and urban air pollution, have also been linked to epigenetic dysregulation [30, 31].

Political instability, conflict, displacement, and climate-related disasters contribute to chronic stress, food insecurity, and disease outbreaks, all of which may induce stress-related epigenetic modifications [29, 31, 32]. These lead to alterations of the hypothalamic–pituitary–adrenal axis that can persist across generations [29, 31, 32]. Another potential contributor is chronic exposure to Shiga-producing and colibactin-producing *Escherichia coli*, which are prevalent across Africa and can induce DNA damage and subsequent epigenetic alterations [33–36]. The colonization may begin at birth through maternal transmission [33–36]. While many lower-incidence countries experience similar challenges, differences in political stability, good nutrition, less environmental exposure, biodiversity, and urbanization may influence the cumulative burden of epigenetic stressors [37–39]. Although causality has not been established, these interacting factors provide a biologically plausible explanation for regional variation in pediatric CRC incidence and differences observed between adult and childhood disease patterns.

This study is limited by its retrospective nature and the small cohorts in some calculations, which requires evaluation of *p*-values with caution. For this reason, the value of immunotherapies could not be clearly evaluated.

5 | Conclusion

CRC in African children has similar disease phenotypes to adult-type tumors due to various factors, many of which are only postulates. Most importantly, complete surgical resection emerged as the only independent predictor of outcome, underscoring the critical role of timely diagnosis and access to curative surgery. Collectively, these findings emphasize systemic gaps across the diagnostic, surgical, and follow-up continuum of care for pediatric CRC in Africa. Addressing these gaps will require improved awareness, earlier referral pathways, strengthened multidisciplinary collaboration, and continent-wide strategies tailored to rare pediatric solid tumors and increasing adult-type tumors presenting in childhood.

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The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

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Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Table S1:** Sensitivity or stratified analysis of the patient characteristics, tumor characteristics and survival outcomes between the Egyptian and non-Egyptian cohorts.

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