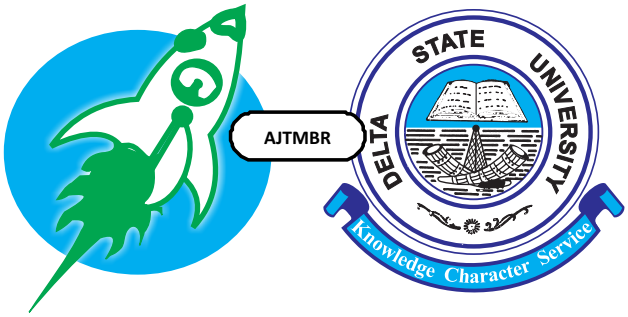
African Journal of Tropical Medicine and Biomedical Research (AJTMBR)



The Journal is the Official Publication of the College of Health Sciences, Delta State University, Abraka, Nigeria.

ISSN: 2141-6397

Vol. 7, No. 2, December 2024

Focus and Scope

The African Journal of Tropical Medicine and Biomedical Research is a multidisciplinary and international journal published by the College of Health Sciences, Delta State University of Abraka, Nigeria. It provides a forum for Authors working in Africa to share their research findings on all aspects of Tropical Medicine and Biomedical Sciences and to disseminate innovative, relevant and useful information on tropical medicine and biomedical sciences throughout the continent. The journal will publish original research articles, reviews, editorials, commentaries, short reports, case reports and letters to the editor. Articles are welcome in all branches of medicine and dentistry including basic sciences (Anatomy, Biochemistry, Physiology, Pharmacology, Psychology, Nursing etc) and clinical sciences (Internal Medicine, Surgery, Obstetrics and Gynaecology, Dental surgery, Child Health, Laboratory Sciences, Radiology, Community Medicine, etc). Articles are also welcome from social science researchers that document the intermediating and background social factors influencing health in countries of Africa. Priority will be given to publication of articles that describe the application of the principles of primary health care in the prevention and treatment of diseases.

Editorial Notices

The journal will be published biannually in the months of March and September. Annual subscription fee in Nigeria is two thousand naira (N2,000) per volume (2issues); One-thousand-naira single copy (N1000). The annual subscription rate for other parts of the world is as follows: United Kingdom £60 (post free). West Africa $60 (post free). The rest of the World and the United States of America $120 (post free). A charge of $60 is made for reprints inclusive of postage. Cheques should made payable to the African Journal of Tropical Medicine and Biomedical Research and addressed to the Editor-in-Chief.

Journal Contact

All correspondence, including manuscripts for publication (in triplicate) should be addressed to:

Professor P.S. Igbigbi
The Editor-in-Chief,
Department of Anatomy,
Faculty of Basic Medical Sciences,
College of Health Sciences,
Delta State University, Abraka,
Delta State, Nigeria.

Or:
Professor Lawrence Omo-Aghoja
Editor
Department of Obstetrics and Gynecology,
Faculty of Clinical Medicine,
Delta State University, Abraka, Nigeria.
Email: journalajtmbr@yahoo.com
Cc: all email to
eguono_2000@yahoo.com
Tel: 08039377043

All authors are advised to submit an electronic copy in CD-ROM along with a hard copy of their manuscript, as this will spare remarkable time in the reviewing and typesetting processes.

In the alternative, authors can submit their articles and covering letter by email attachments. A covering letter (signed by all authors) accompanying the manuscript should certify that the article has not been previously published and is not being considered for publication elsewhere.

Information for Authors

All manuscript are peer-reviewed and accepted with the understanding that the work has not been published or being considered for publication elsewhere. Indeed, the authors would be requested

to sign a copyright form transferring the ownership of the paper to the African Journal of Tropical Medicine and Biomedical Research. All articles must include the correct names and addresses of author(s) including e-mail addresses and telephone numbers. Articles will be subjected to a thorough peer review process before any decision is made to publish or not. Authors should note that the African Journal of Tropical Medicine and Biomedical Research is not under any obligation to publish articles submitted, as decision to publish will be based on recommendations of reviewers and the editorial advisory board.

Manuscripts

Articles submitted for publication should be typed double-spaced with 2.5cm margins with accompanying CD-ROM in Microsoft Word format for easy and quick peer review and typesetting. Each of the following sections should begin in a new page: title page, abstract, introduction, materials and methods, results, discussion, acknowledgment (s), references, tables, legends to figures and illustrations. The manuscript should include:

Title Page

The title page should include the following information: 1. the title and sub-title; 2. the name(s) of the author(s); 3. the affiliation(s) of the author(s); 4. name and address of the corresponding author and 5. three to six key words for indexing and retrieval purposes.

Abstract

The abstract should be structured and not more than 250 words. It should carry the following headings: Introduction, Materials and Methods, Results and Conclusion.

Original Research- The journal welcomes articles reporting on original research, including both quantitative and qualitative studies. Full-length articles should generally not exceed 3000 words, excluding abstract, tables, figures, and references. The subject matter should be organised under appropriate headings and sub-headings as itemized above.

Review Articles- Comprehensive review articles on all aspects of tropical medicine and biomedical sciences will also be considered for publication in the journal. Reviews should provide a thorough overview of the topic and should incorporate the most current research. The length of review articles must not exceed 3,000 words and the organisational headings and sub-headings used are at the author's discretion.

Short Reports - Brief descriptions of preliminary research findings or interesting case studies will be considered for publication as short reports. The length of the abstract and article should be restricted to 150 and 2,000 words respectively and organisation of short reports are left to the author's discretion.

Commentaries or Editorials- Commentaries or editorials on any aspect of tropical medicine and biomedical sciences in Africa will be considered for publication in the journal. Opinion pieces need not reference previous research, but rather reflect the opinions of the author(s). The length should not exceed 2,000 words.

Tables and Figures

All tables and figures should be submitted on separate sheets of paper and should be clearly labelled. Coloured tables and figures may be reprinted in black and white. Authors should especially take care that all tables are clear and understandable by themselves, independent of

the text. A reader should be able to read only the tables and easily grasp all information without the text.

Acknowledgments

Acknowledgments should be included on a separate sheet of paper and should not exceed 100words. Funding sources should be noted here.

References

References should be in the Vancouver style and numbered consecutively in the order in which they are mentioned in the text. Titles of journals should be abbreviated according to the Index Medicus style. Authors must cross-check and make sure that all information provided in the reference list is complete and correctly written. Reference numbers should be inserted above the line on each occasion a reference is cited in the text, e.g., … as 1-3 reported in other studies. Numbered references should appear at the end of the article and should include the names and initials of all authors. The format of references should be as published by the International Committee of Medical Journal Editors in the British Medical Journal 1988, volume 296, pages 401-405. The following are sample references for an article published in a journal and for a book: Ahmed Y, Mwaba P, Chintu C, Grange JM, Ustianowski A, Zumla A. A study of maternal mortality at the University Teaching Hospital, Lusaka, Zambia: the emergence of tuberculosis as a major non-obstetric cause of maternal death. Int J Tuberc Lung Dis 1999; 3: 675-680. Whitby LG, Smith AF, Beckett GJ. Enzyme Tests in Diagnosis. In: Lecture Notes on Clinical Chemistry. Whitby LG, Smith AF & Beckett GJth (eds). 4 editions. Blackwell Scientific Publications. 1988. 103-127.

Units of Measurement

All measurements should be expressed in SI (Systeme International) Units.

Galley proofs

Corrections of galley proofs should be strictly restricted to Printer's error only. Orders for offprints should be made when the corrected proofs are being returned by the authors. Articles accepted for publication remain the property of the journal and can only be reproduced elsewhere in line with section 5 of the copyright agreement.

Table of Contents

Original Articles

Socio-clinical and Immuno-inflammatory-related differences between early-onset and late-onset colorectal cancer

*Okoye JO,[1] * Chiemeka ME,[2] Menkiti FE,[2] Ihekwoaba EC,[3] Agbakoba N,[1] Orwa J[4]*

Abstract

Introduction: This study aimed to identify socio-clinical and immuno-inflammatory markers of early-onset colorectal cancer (CRC) for early detection of aggressive cancer in Southern Nigeria

Material and Methods: This study included 89 patients with CRC diagnosed from Jan. 2016 to Dec. 2022. The patients were sub-grouped based on age and chemotherapy response. The neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), platelet-to-lymphocyte ratio (PLR), platelets-neutrophils-to-lymphocytes ratio (PNLR), and neutrophils-to-lymphocytes platelets ratio (NLPR) were assessed and analyzed accordingly. Significance was set at $p< 0.05$.

Results: Metastatic and stage III/IV CRCs were prevalent among patients older than 50 years compared with patients aged 50 years or less ($p< 0.05$). Among patients aged > 50 years, the pre-treatment (pre-T) to post-treatment (post-T) total white blood cell count (TWBC), neutrophils, monocytes, and NLPR significantly increased whereas the post-T lymphocyte count and LMR significantly declined ($p< 0.05$). The Post-T TWBC count was significantly higher among patients aged > 50 years ($14.20 \pm 4.50\ 10^{\wedge 9}$/L) compared with patients 50 years old or younger ($9.19 \pm 1.50\ 10^{\wedge 9}$/L) whereas the Post-T monocyte count and LMR were lower among the former (9.12 ± 2.33 and 2.87 ± 0.60) than the post-T values of patients who were ≤ 50 years old (11.81 ± 3.57 and 6.76 ± 3.92) at $p= 0.033$, 0.026, and 0.001, respectively.

Conclusion: This study revealed a higher frequency of CRC and mortality risk among patients older than 50 years. It suggests that SIII could be used as a prognostic tool for CRC.

Keywords: Haematological indices, gastrointestinal cancer, Immune cells, Chemotherapy, Southern Nigeria

1Department of Histopathology, Faculty of Medical Laboratory Science, Nnamdi Azikiwe University, Nigeria.
2Department of Morbid Anatomy and Forensic Science, Nnamdi Azikiwe University Teaching Hospital, Nigeria.
3Department of Gastroenterology, Nnamdi Azikiwe University Teaching Hospital, Nigeria.
4Department of Population Health, Aga Khan University, Nairobi, Kenya

Corresponding author: Jude Ogechukwu Okoye. Department of Histopathology, Faculty of Medical Laboratory Science, Nnamdi Azikiwe University, Nigeria.

INTRODUCTION

According to the GLOBACAN 2020 estimates, colorectal cancer (CRC) is the third most common cancer and the second leading cause of cancer-related deaths in the world.[1] The average age-standardized incident rate per 100,000 (ASIR) of colon cancer (CC) in Europe, America, Asia, and Africa were 22.4, 13.0, 10.3, and 5.1, respectively.[1] Comparison of incidence-to-mortality revealed lower case fatalities in countries with a high/very high human development index (HDI) compared with countries with a low/medium HDI; 43.6% vs 62.3%.[1,2] Reasons for the difference between the two HDIs may be due to differences in the stage at presentation, access to healthcare facilities, and affordability of chemotherapy.[3] Another reason of note is that CRCs in Africa are very aggressive

and unusually metastatic.[4,5] In Nigeria, for instance, evidence shows that 34%, 70%, and 96%, of CRCs are poorly differentiated, right-sided (RCC), and invasive, respectively.[3,6] The RCCs are larger, more advanced, and poorly differentiated compared with the left CCs, and patients with RCCs are older.[7-9] RCC patients have poorer overall survival (OS) and disease-free survival (DFS) rates compared with LCC patients.[9] These factors reveal the importance of identifying affordable procedures and biomarkers for CRC that are alternatives to the expensive repeated imaging for high-mortality risk patients who are in low-resource settings. One such approach is precision medicine, in which the assessment of systemic immune-inflammatory (SIII) biomarkers has emerged as a promising option.[10] High pretreatment inflammatory indices have been associated with both a greater risk of cancer relapse in radically resected tumours and shorter survival for cancer patients with metastatic disease.[11] The circulating high neutrophil and low lymphocyte counts, especially post-chemotherapy, are independently associated with poor OS and progression-free survival (PFS), especially in metastatic CRC patients.[12] A low lymphocyte–monocyte ratio (LMR < 2.82), can reflect an active inflammation status and has been associated with high-grade tumours and worse OS and DFS and is more likely to be left-sided.[12] This study assessed the clinical utility and prognostic value of inflammation-related markers for better stratification of CRC patients in Southern Nigeria.

METHODS

Study Population and Ethics

From January 2016 to December 2022, 98 patients with gastrointestinal diseases presented at the Department of Gastroenterology, Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nigeria. Patients with inadequate records, especially haematological parameters (n=9) were excluded from the study. Finally, this study included a total of 89 patients diagnosed with CRC who were living in Anambra State. In addition to some antibiotics and surgeries, some patients received capecitabine and oxaliplatin as platinum chemotherapy. This retrospective study was approved by the NAUTH ethics committee (NAUTH/CS/66/VOL.15/VER.3/107/2022/081). The medical records of the patients were accessed for socio-clinical demographics such as age, gender, comorbidities, time of presentation, time of death, and contact for follow-up. All analyses were performed by the ethical standards laid down in the Declaration of Helsinki.

Sample collection and handling

Peripheral whole blood samples (5 ml each) were collected into EDTA containers one week before the first chemotherapy and a week before discharge. Full blood counts were carried out on the whole blood samples using a Haemo-autoanalyzer. Following ultrasound investigations, sections from biopsies or resected tissues were reviewed for evidence of malignancy and metastasis. The neutrophil, lymphocyte, platelet, monocyte, and total white cell counts ($10^{\wedge 9}$/L) were assessed. Overall survival was calculated from the date of presentation or diagnosis to the date of death or last follow-up. The blood neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), platelet-to-lymphocyte ratio (PLR), platelets-neutrophils to lymphocytes ratio (PNLR; [Platelet count x Neutrophil count]/Lymphocyte count), and neutrophils-to-lymphocytes-platelets ratio (NLPR; [Neutrophil count x 100]/Lymphocyte count x platelet count]).

Study design

The cases of CRC were categorized based on the following: 1. Age (≤ 50 years or > 50 years), 2.

Chemo-sensitive and chemo-resistance. The assessment of features such as the alleviation of symptoms, liver and renal function tests, tumour response or degree of tumour shrinkage, and the need for second-line chemotherapy determined chemoresistance.[13]

Statistical analysis

Chi-square/Fisher was used to determine the association between age and socio-clinical demographics of the patients. Pearson's correlation was used to determine the relationship between the variables (NLR, PLR, PNLR, NLPR, and LMR) before and after the last treatment. A T-test was used to compare data of 1. patients aged ≤ 50 years and > 50 years, 2. chemotherapy naïve and experienced patients. The overall survival of patients was analyzed using the Kaplan-Meier method. The survival probabilities between the subgroups were compared using the log-rank test.

RESULT

The mean age, median age, and age range of the participants were 56.40 ± 13.58 years, 58.0 years, and 25 to 92 years, respectively.

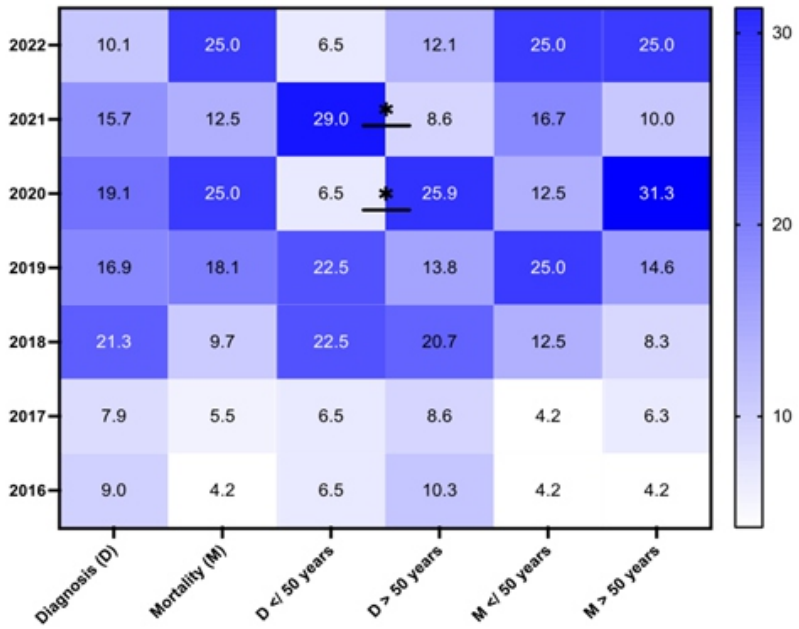


Figure 1: Heatmap of the percentage diagnosis (D) and mortality (M) rate among CRC patients aged ≤ 50 years and > 50 years

There was a high number of CRC diagnoses in 2018 (21.3%) compared with other years while a high rate of mortality was observed in 2020 (25.0%) and 2022 (25.0%) compared with other years. The prevalent features presented by the patients were: Weight loss, constipation, intermittent diarrhoea, low abdominal pain, and anorexia (see supplementary file). In 2020, the CRC diagnosis and mortality rates were approximately 4 times and 2.5 times higher among patients aged > 50 years compared with patients whose ages were less than or equal to (</;

≤) 50 years at p= 0.045 and 0.147, respectively. In 2021, the rate of CRC diagnosis was 3.4 times higher among patients who were ≤ 50 years old compared with those aged > 50 years at p= 0.016 (figure 1).

Table 1: Socio-clinical characteristics of CRC patients in NAUTH

Variables	**No. (%) N= 89**	**≤ 50 years n= 31 (%)**	**>50 years n= 58 (%)**	**p- value**
Sex				0.266
Male	43 (48.3)	12 (38.7)	31 (53.4)	
Female	46 (51.7)	19 (61.3)	27 (46.6)	
Employment status:				0.325
Civil servant	22 (24.7)	7 (22.6)	15 (25.9)	
Dependant	15 (14.6)	3 (9.7)	12 (20.7)	
Self employed	52 (58.4)	21 (67.7)	31 (53.4)	
Level of Education:				0.034*
No formal education	5 (5.6)	0 (0.0)	5 (8.6)	
Basic education	52 (58.4)	15 (45.5)	37 (63.8)	
Tertiary education	32 (36.0)	16 (50.0)	16 (27.6)	
Alcohol consumption:				0.658
No	44 (49.4)	14 (45.2)	30 (51.7)	
Yes	45 (51.6)	17 (54.8)	28 (48.3)	
Tobacco Use:				0.746
No	77 (86.5)	26 (83.9)	51 (87.9)	
Yes	12 (13.5)	5 (16.1)	7 (12.1)	
History of Hypertension:				0.500
No	56 (62.9)	18 (58.1)	38 (65.5)	
Yes	33 (37.1)	13 (41.9)	20 (34.5)	
History of Herbal therapy:				0.999
No	77 (86.5)	27 (87.1)	50 (86.2)	
Yes	12 (13.5)	4 (12.9)	8 (13.8)	

TSMP:				0.077
> 12 months	17 (19.1)	9 (29.1)	8 (13.8)	
7-12 months	33 (37.1)	13 (41.9)	20 (34.5)	
≤ 6 months	39 (43.8)	9 (29.0)	30 (51.7)	
Tumour site:				0.698
Right-sided Colon	25 (28.1)	7 (22.6)	18 (31.0)	
Left-sided Colon	27 (30.3)	10 (32.3)	17 (29.3)	
Rectum/Recto-sigmoid	37 (41.6)	14 (45.1)	23 (39.7)	
Metastasis				0.002*
No	59 (66.3)	27 (87.1)	32 (55.2)	
Yes	30 (33.7)	4 (12.9)	26 (44.8)	
Chemotherapy experience:				0.026*
No	52 (58.4)	13 (41.9)	39 (67.2)	
Yes	37(41.6)	18 (58.1)	19 (32.8)	
Tumour grade				0.052*
Well differentiated	37 (41.6)	9 (29.0)	28 (48.3)	
Moderately differentiated	43 (48.3)	16 (51.6)	27 (46.5)	
Poorly differentiated	9 (10.1)	6 (19.4)	3 (5.2)	
Histologic type				0.023*
Adenocarcinoma	66 (74.2)	19 (61.3)	47 (81.0)	
Squamous cell carcinoma	17 (19.1)	7 (22.6)	10 (17.2)	
Others	6 (6.7)	5 (16.1)	1 (1.8)	
Disease Stage				0.006*
Stage 1	34	15 (48.4)	19 (32.8)	
Stage 2	25	12 (38.7)	13 (22.4)	
Stage 3	13	4 (12.9)	9 (15.5)	
Stage 4	17	0 (0.0)	17 (29.3)	

TSMP: Time of symptom manifestation to presentation. Descriptive analysis and Chi-square/Fisher's exact test. *Significance was set at $p < 0.05$.

Age-related differences among CRC patients

The prevalence of CRC was slightly higher among females compared with men, especially among those who were under 50 years of age (Table 1). RCCs and metastasis were prevalent among patients who were over 50 years old whereas rectal tumours were prevalent in patients who were ≤ 50 years (p> 0.05). Less than 50% of the patients received chemotherapy and a higher percentage of those patients were under 50 years (p= 0.05). No significant difference was observed between the two age groups in terms of the history of herbal therapy use. The level of tertiary education was higher among patients who were ≤ 50 years compared with their over 50 years counterparts (p< 0.05). The history of tobacco use, alcohol consumption, and hypertension was prevalent among patients who were aged ≤ 50 years compared with their > 50 years counterparts (p> 0.05). Patients who were aged > 50 years old were approximately 1.8 times more likely to present at the clinic in ≤ 6 months of symptom development compared with their 50-year counterparts (p= 0.046). The rate of unemployment was lower among patients who were older than 50 years compared with their 50-year counterparts (p> 0.05). The patients who were 50 years old and under had higher tumours grade than patients who were older than 50 years (p< 0.05). Based on histology, the prevalence of adenocarcinoma was higher among patients aged > 50 years compared with patients aged ≤ 50 years (p< 0.05). The rate of surgical resection uptake was higher among patients aged > 50 years (58.6%) compared with their ≤ 50 counterparts (54.8%) at p= 0.823. Post-T TWBC count was 1.5 times higher among patients who were above 50 years compared with their 50-year counterparts (p< 0.05) while the post-T monocyte and LMR were also lower among the former than the latter at p< 0.05 (table 2). Among patients aged ≤ 50 years, only the post-T monocyte significantly increased compared with the pre-T values at p< 0.05 (table 2). Among patients aged > 50 years, the post-T TWBC, neutrophils, monocytes, and NLPR values significantly increased whereas the post-T lymphocyte and LMR significantly reduced compared with the pre-T values (p< 0.05).

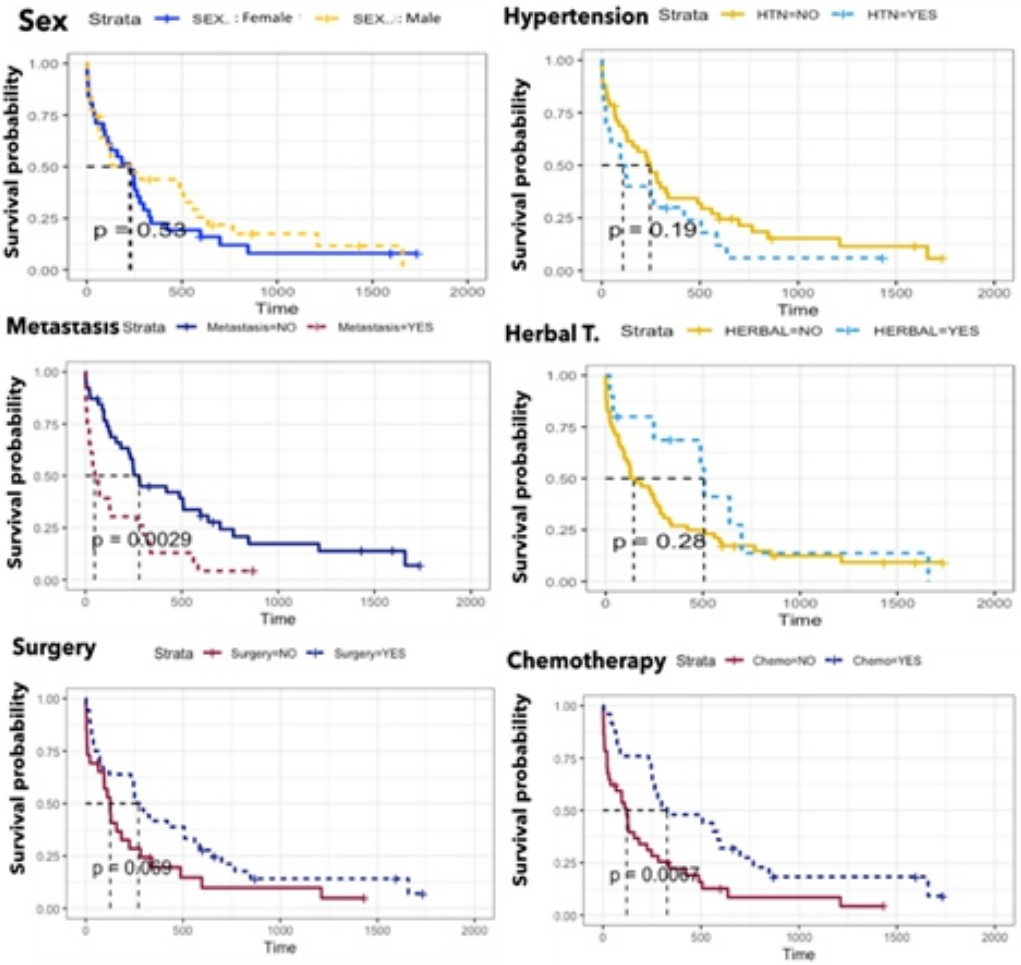


Figure 2: Survival analysis of CRC patients based on sex, history of hypertension and herbal therapy, uptake of surgery, chemotherapy, and occurrence of metastasis (Kaplan–Meier curve)

Figure 2 shows that patients with non-metastatic CRC lived longer than their counterparts (mean = 594.6 days vs 268.2 days, respectively; $p< 0.05$). Those who were chemo-experienced also lived longer than their chemo-naïve counterparts (mean = 524.3 days vs 205.2 days, respectively; $p< 0.05$). Patients with surgical resections lived longer than their surgery-naïve counterparts (mean = 487.8 days vs 280.7 days, respectively; $p> 0.05$). More so, normotensive patients lived longer compared with patients with a history of hypertension (mean = 454.1 days vs 288.0 days, respectively; $p> 0.05$). The figure also shows that males lived longer than their female counterparts (mean/median= 462.2/233 days vs 344.8/225 days, respectively; $p> 0.05$). Interestingly, patients with a history of herbal therapy lived longer compared with herbal therapy-naïve patients (mean/median= 581.3/506.0 days vs 374.2/145 days, respectively; $p> 0.05$). Patients who presented at the clinic between 7 to 12 months of symptom development had a higher mean survival rate (207.0 ± 55.3/192.2 days) compared with those presented at > 12 (197.5 ± 34.9/172.6 days) and ≤ 6 months (182.6 ± 35.1/45.3 days) at $p= 0.820$. Patients without a history of tobacco use and alcohol consumption lived longer (mean/median= 162.8 ± 37.2/39 days and 159.5 ± 50.0/35 days) than those with a history of the lifestyles (98.2 ± 38.3/15 days and 135.8 ± 34.3/43 days) at $p= 0.200$ and 0.580, respectively. Surprisingly, the mean/median survival rate among patients with DM (n= 12) was higher (629.0 ± 185.7/506.0 days) compared with those without the disease (373.2 ± 71.2/145 days, respectively) at $p= 0.190$ (see supplementary file).

Chemotherapy-associated Survival analysis

The overall mortality rate was 91.8%. Based on follow-up, the two-year and four-year survival rates of the patients were 5.2% and 3.9%, respectively. Chemo-experienced patients and patients who had non-metastatic tumours lived longer than chemo-naïve and patients with metastatic tumours (figure 2). A significant inverse relationship was observed between metastasis and survival (p= 0.001). The in-hospital mortality rate was higher among cases with metastasis (46.2%) compared with non-metastatic cases (13.7%). Based on the survival rate, no significant difference was observed between chemo-experienced and herbal-experienced patients at p= 0.263. Patients without a history of tobacco use, and alcohol consumption lived longer (162.7 days and 159.5 days) compared with the history (mean = 98.2 days and 135.8 days, respectively; p> 0.05). Patients who were both herbal and chemo-experienced had a higher mean survival rate (n= 2; 613 ± 76.50 days) compared with herbal/chemo-naïve patients (n= 42; 51.91 ± 14.61 days) at p< 0.001. Only 54.1% (n= 20) of the chemotherapy-experienced patients had 6 courses of chemotherapy; chemo-resistant patients (Chemo-R.; 30%) = 6 and chemo-sensitive (Chemo-S.; 70%)= 14.

Table 2: Comparative analysis of haematological indices between two age groups

Variable		≤ 50 years n= 31	> 50 years n= 58	*P* -value
		Mean ± SD	**Mean** ± SD	
WBC (10^9/L) BT		8.38 ± 0.90	8.37 ± 1.09	0.580
WBC (10^9/L) AT		9.19 ± 1.50	14.20 ± 4.50	0.033*
	P- value	0.560	0.017*	
Lymphocyte (%) BT		36.40 ± 3.60	34.12 ± 3.60	0.203
Lymphocyte (%) AT		31.03 ± 4.11	27.05 ± 7.40	0.056
	P- value	0.240	0.031*	
Neutrophil (%) BT		52.38 ± 4.09	51.70 ± 5.05	0.783
Neutrophil (%) AT		46.14 ± 7.54	57.33 ± 10.26	0.138
	P- value	0.287	0.016*	
Platelet (10^9/L) BT		322.03 ± 32.11	405.08 ± 34.57	0.979
Platelet (10^9/L) AT		376.42 ± 46.84	330.44 ± 33.62	0.316
	P- value	0.820	0.546	

Monocytes (%) BT		7.23 ± 0.77	3.33 ± 0.60	0.138
Monocytes (%) AT		11.81 ± 3.57	9.12 ± 2.33	0.026*
	P- value	0.026*	0.018*	
NLR BT		2.12 ± 0.36	2.50 ± 0.56	0.260
NLR AT		2.83 ± 0.74	3.23 ± 1.07	0.831
	P- value	0.197	0.236	
PLR BT		173.5 ± 23.83	204.4 ± 37.98	0.621
PLR AT		193.0 ± 55.00	219.5 ± 45.51	0.849
	P- value	0.754	0.802	
PNLR BT		830.63 ± 212.89	1225.08 ± 232.1	0.316
PNLR AT		953.90 ± 325.32	1385.67 ± 211.3	0.102
	P- value	0.901	0.518	
NLPR BT		0.84 ± 0.15	0.57 ± 0.12	0.307
NLPR AT		1.12 ± 0.32	1.08 ± 0.33	0.736
	P- value	0.154	0.007*	
LMR BT		15.93 ± 4.01	8.73 ± 2.23	0.397
LMR AT		6.76 ± 3.92	2.87 ± 0.60	0.001*
	P-value	0.388	< 0.001*	

Keys: BT; before treatment, AT; after treatment. Statistics: T-test. *Significance was set at $p < 0.05$.

DISCUSSION

In this study, we analyzed the levels of systemic immune-inflammatory indices as an alternative and cost-effective tool for monitoring CRC patients at high mortality risk, especially those in low/medium HDI countries. First, this study revealed that the frequency of the diagnosis and mortality rate significantly increased among the former at the peak of the COVID-19 pandemic, 2020, possibly due to limited access to health facilities at the time. This study also revealed that the disease was more prevalent among patients

above the age of 50 years (58%) than in patients who were 50 years and below. This aligns with the study carried out by Alatise *et al.* and by Saluja *et al.* who investigated 347 and 160 cases of CRC in Western Nigeria and observed that the disease was dominant among patients aged > 50 years (62.8% and >50%, respectively).[3,14] The findings of this study are at variance with two other studies carried out in Northern Nigeria, one of 50 cases and one of 605 cases, reported 72% and 62.6% disease dominance among patients aged 50 years.[15,16]

Regarding tumour sites, this study revealed a lower frequency of RCCs (48.1%) compared to LCCs (51.9%). This is discordant with the findings of Edino *et al.* and Theyra-Enias *et al.* who reported a high frequency of RCC (77.8% and 55.6%) compared with LCC (22.2% and 44.4%) in Northern Nigeria from 1999 to 2015.[15,17] This study is also at variance with the findings of Alatise *et al.* who observed a high frequency of RCC (80%) in Western Nigeria compared with LCC (20%).[3] The findings of this study in terms of tumour sites align with the findings of Saluja *et al.* who reported a lower frequency of RCC (47.6%) compared with LCC (52.4%) in Western Nigeria.[14] This suggests that the CRCs in Northern Nigeria are more lethal than those observed in Southern or Western Nigeria. The reason for the variation and similarities between the regions is unknown but it could be related to diet, lifestyle, or rate of genetic mutations.[18]

The findings of Irabor *et al.* are very similar to the findings of this study in terms of sex and age-related differences in tumour site and grade.[6] They reported a lower RCC frequency but higher frequencies of poorly differentiated adenocarcinoma and rectal tumours among patients aged 50 years (15%, 43%, and 72%) compared with their > 50 years counterparts (32%, 27%, and 59%, respectively). Additionally, Irabor *et al.* reported a higher frequency of the disease among females and males who were aged ≤ 50 years (62%) and > 50 years (56%), respectively.[6] The prevalent tumour grades in the study carried out by Edino *et al.* and Alatise *et al.* were poorly differentiated adenocarcinoma (34%) and moderately differentiated adenocarcinoma (55.3%), respectively whereas well-differentiated adenocarcinoma was prevalent among the patients of this study.[3,15] The high frequency of rectal tumours and poorly differentiated adenocarcinoma among patients aged 50 years could be due to a high frequency of history of tobacco use, and alcohol consumption. This may affect the clinical outcomes of the patients. Previous studies show that RCC is associated with lower survival compared with LCC due to its metastatic potential, microbiome changes, and high microsatellite instability; MSI-high.[6,19] This might be the reason for the higher rate of metastasis among patients older than 50 years in this study.

The number of patients who received chemotherapy in this study is lower than the frequency recorded by Edino *et al.* and Theyra-Enias *et al.* in Northern Nigeria (94% and 73%, respectively).[15,17] and the frequency of 67.5% and 50.5% recorded by Saluja *et al.* and Sharma *et al.* in Western Nigeria.[14,20] The reasons for low chemotherapy uptake are due to patients' reasons, side effects, and lack of funds.[17] Even though our findings and that of Edino *et al.* are fourteen years apart, both studies revealed that most of the CRC patients in Nigeria present after 6 months of symptom development.[15] This might be the explanation for the higher frequency of metastasis among our cohort and high mortality among Nigerian patients. This suggests that the level of awareness and knowledge of the disease is quite low.

Based on the time of presentation at the clinic, the NLR value shows that patients who presented after 6 months of symptom manifestation were at a higher risk of mortality at presentation than patients who presented within 6 months of symptom manifestation. Even though most of the patients aged > 50 years presented at the clinic within 6 months of symptom development, they had a higher frequency of metastasis and stage III/IV CRC compared with their ≤ 50-year-old counterparts. Despite surgical resections in this group, the three-fold reduction in post-T NLPR was mitigated by the four-fold decrease in post-T LMR. The significant increase in post-T total WBC, neutrophil, monocytes, NLPR, and a significant decrease in lymphocyte, and LMR suggests that patients aged > 50 years responded poorly to treatment due to age-related physiologic limitations. In China, patients with NLR>2.72, PLR>219.00, and LMR≤ 2.83 were significantly associated with decreased OS and DFS.[21] In this study, these features were seen among patients aged > 50 years. Thus, the low uptake of chemotherapy by patients aged > 50 years may be responsible for their high mortality rate in 2020. More so, the high NLR and low LMR among our cohort could be the reason for the high in-hospital death in this study.

CONCLUSION

This study shows that age is a strong driver of disease aggressiveness among patients in Southern Nigeria. It revealed that NLR, PLR, LMR, and PNLR values provide affordable insights into treatment outcomes, especially among elderly patients with late-stage diseases. There is a need for increased awareness and closer follow-up among patients aged 50 years and above. Due to the high prevalence of early-onset CRC in West Africa, this study suggests that screening for CRC should begin at 40 years.

Conflict of Interest

The authors have declared no competing interests.

Contributions to joint publication

Author JOO conceptualized and designed the study. Authors JOO, CME, MFE, IEC, and NR collected, collated, and interpreted the data. Authors JOO and JO analyzed the study. All authors have read and approved the final version.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: Cancer J Clin. 2021;71(3):209-49. Doi: 10.3322/caac.21660
2. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global patterns and trends in colorectal cancer incidence and mortality. Gut. 2017;66(4):683-91. doi:10.1136/gutjnl-2015-310912
3. Alatise OI, Knapp GC, Bebington B, Ayodeji P, Dare A, Constable J, *et al*. Racial Differences in the Phenotype of Colorectal Cancer: A Prospective Comparison Between Nigeria and South Africa. World J Surg. 2022;46:47-53. Doi: 10.1007/s00268-021-06304-z
4. Irabor DO, Afuwape OO, Ayandipo OO. The present status of the management of colon and rectal cancer in Nigeria. J Cancer Res. 2014. Doi: 10.1155/2014/267190.
5. Alatise OI, Kingham TP. African Research Group for Oncology and MSKCC Global Cancer Disparity Initiative team. Abstract LB-327: Colorectal cancer in Nigeria: High tech and low-tech approaches to improving patient outcomes. Cancer Res. 2019;79(13_Supplement):LB-327. Doi:10.1158/1538-7445.AM2019-LB-327

6. Irabor DO, Oluwasola OA, Ogunbiyi OJ, Ogun OG, Okolo CA, Melas M, *et al.* Microsatellite instability is common in colorectal cancer in native Nigerians. Anticancer Res. 2017;37(5):2649-54. Doi: 10.21873/anticanres.11612.
7. Tejpar S, Stintzing S, Ciardiello F, Tabernero J, Van Cutsem E, Beier F, *et al.* Prognostic and predictive relevance of primary tumor location in patients with RAS wild-type metastatic colorectal cancer: retrospective analyses of the CRYSTAL and FIRE-3 trials. JAMA Oncol. 2017;3(2):194-201. doi:10.1001/jamaoncol.2016.3797
8. Kim K, Castro EJ, Shim H, Advincula JVG, Kim YW. Differences regarding the molecular features and gut microbiota between right and left colon cancer. Ann Coloproctol. 2018;34(6):280. Doi: 10.3393%2Fac.2018.12.17
9. Guo D, Li X, Xie A, Cao Q, Zhang J, Zhang F, *et al.* Differences in oncological outcomes and inflammatory biomarkers between right-sided and left-sided stage I-III colorectal adenocarcinoma. J Clin Lab Anal. 2020;34(4):e23132. Doi: 10.1002/jcla.23132
10. Pérez-Martelo M, González-García A, Vidal-Ínsua Y, Blanco-Freire C, Brozos-Vázquez EM, Abdulkader-Nallib I, *et al.* Clinical significance of baseline Pan-Immune-Inflammation Value and its dynamics in metastatic colorectal cancer patients under first-line chemotherapy. Sci Rep. 2022;12(1):6893. doi: 10.1038/s41598-022-10884-8
11. Rossi S, Basso M, Strippoli A, Schinzari G, D'Argento E, Larocca M, *et al.* Are markers of systemic inflammation good prognostic indicators in colorectal cancer?. Clin Colorectal Cancer. 2017;16(4):264-74. doi: 10.1016/j.clcc.2017.03.015.
12. Yamamoto T, Kawada K, Obama K. Inflammation-related biomarkers for the prediction of prognosis in colorectal cancer patients. Int J Mol Sci. 2021;22(15):8002. Doi: 10.3390/ijms22158002
13. Watanabe H, Okada M, Kaji Y, Satouchi M, Sato Y, Yamabe Y, *et al.* New response evaluation criteria in solid tumours-revised RECIST guideline (version 1.1). Gan to kagaku ryoho. Cancer Chemother. 2009;36(13):2495-501.
14. Saluja S, Alatise OI, Adewale A, Misholy J, Chou J, Gonen M, *et al.* A comparison of colorectal cancer in Nigerian and North American patients: is the cancer biology different? Surg. 2014;156(2):305-10. Doi: 10.1016/j.surg.2014.03.036
15. Edino ST, Mohammed AZ, Chicha O. Characteristics of colorectal carcinoma in Kano. Nigeria: An analysis of 50 cases. Nig J Med. 2005;14(2):161-6.
16. Holowatyj AN, Maude AS, Musa HS, Adamu A, Ibrahim S, Abdullahi, A et al. Patterns of early-onset colorectal cancer among Nigerians and African Americans. JCO Global Oncol. 2020;6:1647-55. Doi:10.1200%2FGO.20.00272
17. Theyra-Enias H, Tumba N, Popoola OB. Management and outcome of colorectal cancer in a resource-limited setting: Ahmadu Bello University Teaching Hospital, Zaria, Nigeria. Nig J Clin Prac. 2022;25(6):923-30. Doi:10.4103/njcp.njcp_1948_21
18. Irabor DO. Diet, environmental factors and increasing incidence of colorectal cancer in Nigeria. Ann Nig Med. 2014;8(2):58-64. DOI: 10.4103/0331-3131.153353
19. Marx O, Mankarious M, Yochum G. Molecular genetics of early-onset colorectal cancer. World J Biol Chem. 2023;14(2):13. doi: 10.4331/wjbc.v14.i2.13
20. Sharma A, Alatise OI, Adisa AO, Arowolo, OA, Olasehinde O, Famurewa, OC, et al. Treatment of colorectal cancer in

Sub-Saharan Africa: Results from a prospective Nigerian hospital registry. J Surg Oncol. 2020;121(2):342-9. Doi: 10.1002/jso.25768

21. Li Y, Jia H, Yu W, Xu Y, Li X, Li, Q, et al. Nomograms for predicting prognostic value of inflammatory biomarkers in colorectal cancer patients after radical resection. Int J cancer. 2016;139(1):220-31. Doi: 10.1002/ijc.30071

Okoye JO, Chiemeka ME, Menkiti FE, Iheakwoaba EC, Agbakoba N, Orwa J. Socio-clinical and Immuno-inflammatory Related Differences between Early-onset and Late-onset Colorectal Cancer. Afr. J. Trop. Med. & Biomed. Res. 2024; 7(2) 58-70
https://dx.doi.org/10.4314/ajtmbr.v7i2.6