

September 22, 2014



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 13053-review.doc).

**Title:** A retrospective study of colorectal cancer in Zimbabwe: colonoscopic and clinical correlates

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**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 13053

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) Reviewer 02445587- The reviewer pointed out that our "CRC is as likely among black Africans as it is amongst Caucasians living in Zimbabwe' could be due to selection bias. We agree with this observation. In the revised manuscript we have made this point clearer. In the discussion we have acknowledged that the findings should be extrapolated to the general population cautiously, since this was a highly selected group.

(2) Reviewer 02458152

The reviewer made a very detailed and comprehensive review for which we are grateful. These have significantly improved our article. We have listed the comments the reviewer made, followed by our response for each comment for clarity:

i) Abstract

Objective:

This study only compared differences in the frequency of colorectal cancer according to ethnicity. Please, delete..... describe the findings during colonoscopy in Zimbabwe.

*Response*

We agree our article does not focus on the other findings in depth and have deleted the line in the abstract as suggested.

ii) Core Tip

1. The use of mean age does not give enough credence to the assertion that African patients are often younger, implying that investigations for colorectal cancer among African populations should be instituted in all patients in the right clinical context regardless of age.

2. The conclusion that 'these young patients may represent hereditary colorectal, suggesting that genetic predisposition drives a significant' .....cannot be drawn from this study and should be deleted.

*Response*

We have compared the differences in age using age categories as the reviewer suggested in subsequent comments. African patients with colorectal cancer were younger even on this analysis so the gist of the core tip was maintained. However we have deleted the conclusion that these young patients represent hereditary colorectal cancer, as the reviewer had quite rightly pointed out that this

cannot be drawn from the study.

iii) Introduction

page#6, para#1, line#2- This statement is deceptive. The claim that environmental exposure serves as a protective agent is not completely true. The authors should specify the environmental hazards the perceived as protective. I am of the view that the rarity of colorectal cancer among blacks may be due to the fact that some patient resorts to other traditional remedies. There may be other issues of accessibility of healthcare for the poor. And healthcare coverage.

*Response*

We agree with the reviewer's comment and have specified that the environmental exposures, which are dietary. We agree with the reviewer that patients often resort to alternative remedies. We had made this point in the opening paragraph, but have changed the wording from the 'unconventional remedies' to 'traditional and faith-based methods for clarity. We agree with the reviewer that access to healthcare may be uneven, and have pointed this out in paragraph 3 of the introduction.

iv) Methods

Predictive as used by the authors is inappropriate. This occurs in several places in the manuscript. I recommend the authors change "predictive" to "association".

*Response*

We agree that the use of the term predictive is inappropriate and have changed it as suggested.

v) pg#8, para#3, line#4 from bottom: I am not sure what the authors mean by colorectal cancer by race is the dependent variable.....The dependent variable is colorectal cancer.

*Response*

We agree with this comment and have made the suggested change.

vi) Results

1. pge#9, para#1, line#2-3: the authors have indicated that repeat procedure was an exclusion criteria "Repeat procedures within the study period were excluded, unless if there was an important new finding or if the procedure was repeated because the initial evaluation was inadequate". So 93 patient were excluded from the analysis not from further analysis

2. pg#9, para#2, line#3-4: the authors were interested in comparing colorectal cancer by age, I propose they should construct age categories which is more informative and intuitive than mean age

3. pge#9, para#3, line#3-4: the results in the tables are not consistent with that in the text. e.g. Both rectal bleeding and anaemia were more common as a reason for undergoing colonoscopy in black African patients than in Caucasians and Asians. This statement is incorrect. In the table the black, Caucasian and Asian anaemia prevalence was 15% vrs. 4% vrs 16%. This problem occurs in several places in the text. (e.g. pg#12, para#2, line#2-3)

4. I am not sure why the authors used the subtitle 'Findings'. It's a bit confusing. When they have used Results somewhere and findings elsewhere. I am sure this follows the Title in Table 3. I recommend they use an appropriate title which reflects the results in the table. They should also change the title of table 3

5. pg#9, para#4, line#2-3: The authors should compare their findings by all ethnic groups as they did in the earlier submission (i.e. by black vrs Caucasian vrs Asian). This inconsistent also occurs in pg#10, para#1.

6. pg#10, para#1: This follows from my earlier comment. The authors should construct age categories for a meaningful comparison by age. They have reported age levels in the text. I suggested they show that in the table.

7. pg#11, para#1, line#7: I didn't see any trend in the table with respect to family history of bowel cancer. Please revise this sentence.

*Response*

- The wording has been changed to reflect that 93 patients were excluded from analysis not from further analysis.
- Age categories have been constructed (Table 5) and they show the differences in age in a much clearer way as the reviewer suggested.
- The inconsistencies in comparisons between clinical features by race between tables and the text are acknowledged and have been corrected.
- The subtitle has been changed from 'Findings' to 'Endoscopic and Histological Diagnoses'. The titles of both Table 3 and Table 4 have been changed to reflect this.
- The findings have been compared among all the three ethnic groups represented in the study in most instances. We have however limited the comparison on the age categories and predictive features to black Africans and Caucasians because there were very few Asians (2) with colorectal cancer in the study and statistical comparisons would be meaningless.
- The age categories have now been tabulated (Table 5).
- The sentence on family history has been revised.

v) DISCUSSION

8. pg#12, para#2, line#3: higher proportion may be true for haematochezia but not for anaemia. Please, revise this sentence.

9. pg#13, para#2'line#1-2: Unless the authors construct age categories, mean age as used in this study does not reflect this assertion

10. pg#13, para#2, line#1-2: May be this population constitute working population and may be exposed to occupational and environmental risk factors for (e.g. pesticides) colorectal cancer.

11. pg#14, para#2, line#1: what do the authors mean by 'unbalanced'? can they use a more clearer term?

12. To what extent have the authors justified both the external and validity of this study to make such a wide generalization? I recommend the authors delete the last 2 lines of the conclusion.

*Response*

- The sentence referring to haematochezia and anaemia has been revised.
- Age categories have been constructed (Table 5) and they show that black patients were younger.
- We agree that it is possible that the young may have been exposed to unique carcinogens by virtue of their comprising the working populations. We have added this to our argument speculating about the potential causes of colorectal cancer in young patients.
- We have changed 'unbalanced' to 'limitations'.
- We agree that it is not possible to make such wide generalisations and have deleted the last 2 lines as suggested by the reviewer.

(3) Reviewer 02467528

*Response*

Thank you for the review. We have gone over the tables as suggested by the reviewer. It should be noted that the percentages in Table 2 do not add up to a 100% because some patients had more than one symptom or indication and are counted more than once. For example you could have someone with both a change in bowel habit and anaemia. We have now clearly stated this below the table so that it is completely clear. We agree with the concern about generalising the findings to the African population at large. This concern has also been raised by reviewers 02458152 and 02445587, and we have addressed this in the discussion under limitations. We have also deleted the last 2 lines of the article which had made the assertion. Similarly we have discussed the limitations inherent in a single centre study as suggested by the reviewer. However, we wish to point out that our centre performed

more than 60% of the lower gastrointestinal endoscopies done in Zimbabwe over this period, so our study captured most of the patients who underwent the procedures. We agree with the point raised by the reviewer that sigmoidoscopy examinations could have resulted in underestimation of disease and have incorporated this in the discussion. The statistical tests used have been stated in the methods section. We had indicated the types of tumours below Tables 3 and 4 in addition to having mentioned them in the text.

(4) Response to reviewer 02475623

Thank you for the review. It is possible that socio-economic status is a confounder and this has been pointed out in the discussion.

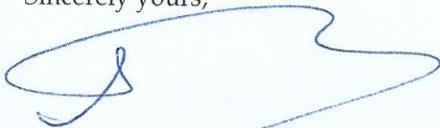
(5) Response to reviewer 02977366

Thank you for the comments. We agree the data came from a single centre, and have discussed this limitation in the discussion. However, our centre saw at least 60% of the patients requiring colonoscopy in Zimbabwe, and thus the data can be taken to be reasonably representative of the country's situation. We did not provide information on the frequency of risk factors of colorectal cancer between the different ethnic groups as this was not the focus of our study. Rather, we sought to describe the frequency with which colorectal cancer is diagnosed on colonoscopy or sigmoidoscopy among different ethnic groups in a country where colorectal cancer is perceived to be rare. Information on the frequency with which risk factors occur between the different groups would be best addressed by a case-control study. We are currently carrying out such a study in our population and have almost completed the recruitment. Table 5 has been added which shows the age categories of our patients and Table 6 provides further clinical information on the cases.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,



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