Author's response to reviews

Title: Utility of serum des-gamma-carboxyprothrombin in the diagnosis of hepatocellular carcinoma among Nigerians, a case-control study.

Authors:

Akpakip I Ette Dr. (draette@yahoo.com)
Dennis A Ndububa Prof. (dennisndububa@yahoo.co.uk)
Olusegun Adekanle Dr. (olusegunadekanle@yahoo.co.uk)
Udeme Ekrikpo Dr. (udekrikpo@yahoo.com)

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The Editor BMC Gastroenterology

Dear Sir/Madam

COVER LETTER FOR REVISED MANUSCRIPT

We are glad to submit our revised manuscript titled, “Utility of serum des-gamma-carboxy prothrombin in the diagnosis of hepatocellular carcinoma among Nigerians, a case-control study” to your highly esteemed journal.

Various revisions have been made to address the concerns of the reviewers as follow:

REVIEWER 1

Q1. The introduction could be supported with more background information on DCP. A few comments were made in the discussion, but more historical information about how it was found and its current use in clinical practice would help clarify the purpose of the study.

ANS: More background information on DCP has been added with a few more references.

Q2. How were patients chosen for the benign liver disease population? More specifically, why include one patient with an amoebic abscess, one with a hepatic cyst and one with acute hepatitis? These processes do not have similar physiology to viral hepatitis and are less likely to result in cirrhosis. Does including these conditions alter the results of the control group?

ANS: The three patients have now been excluded and the analysis repeated using 62 HCC cases and 57 controls.
Q3. What determined which imaging modality was used for patients in the study? Can more information be given about who received a CT or an ultrasound?

ANS: The answer is added under Methodology. All the cases and controls were subjected to Abdominal Ultrasound scans while Abdominal CT scan was restricted to those with focal lesion in the liver.

Q4. How has this study changed your clinical practice? Is DCP used regularly to diagnose your patients with HCC? Should DCP be used in conjunction with AFP? Comments on your clinical practice would be interesting in the discussion.

ANS: The answers are given in the discussion and partly under the results sections;

“It is important to note also that AFP did not correlate with DCP (Spearman rank correlation coefficient=0.12 and p=0.36)“.

“Univariate analysis in this study showed no correlation between DCP and AFP indicating that the combination of these markers is complementary”.

The answer to the question on DCP use in Nigeria is also given in the discussion:

“DCP is not routinely employed for the diagnosis of HCC in Nigeria principally due to unavailability. With the result of this study, a case may now be made for its use as most cases of HCC seen in Nigeria are in the late stages at presentation”.

REVIEWER 2

1. How did HCC cases breakdown? Primary cancers or secondary? Did the cancers metastasize? Hep B was most common etiologic factor. Was there significant difference in AFP and DCP values for HCC cases not caused by Hep B?

ANS: They were all primary cancers. This has now been indicated in the opening part of the sections on Methodology and also Results. One metastasized to the pleura and is now mentioned in the result section. The effect of Hepatitis B infection is analysed in the new table 4 and discussed in the discussion.

2. Was there a correlation between DCP values and the presence of multiple hepatic tumours?

ANS: The Mean ±SD for multiple hepatic tumours and single tumour were analysed and compared to check for any significant difference between the two. The outcome is recorded in the results section.

3. Could DCP be more specific to males instead of females?

A similar analysis as pertains to Q. 2 was repeated for this question.
4. Literature suggests that while DCP is more specific then AFP, AFP remains more sensitive. This is not the case in this study. Why do you think that is?

ANS: The report by Marrero et al (2009) (ref.31), is added to support earlier references in our article. They noted that while the performance of AFP is better than that of DCP for Early Stage HCC the reverse was the case for intermediate-advanced stage HCC and almost all the patients in our study presented in the late stage. Nakamura et al (2006) (ref.17) gave a similar report. We think it is due to late presentation of our patients.

5. DCP is a prothrombin-precursor. Are there dietary considerations in Nigerian culture that could affect these levels? Or individual patient medications?

ANS: The background information section has been fortified with new references to show that the accuracy of DCP results could be diminished by vitamin K deficiency as could be seen in severe malnutrition. It could also be diminished by vitamin K antagonists such as warfarin and also by prolonged obstructive jaundice.

Dear Sir/Madam, apart from addressing the concerns of the reviewers, minor corrections have been made which are mainly typographical and minor correction of addresses.

We wish to thank the editorial team and the reviewers for their erudite and painstaking observations and corrections.

Thank you.

Yours faithfully

Dr. A. Ette

(Corresponding Author)