

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Cross-sectional hospital based-study on the sero-prevalence of Hepatitis B virus markers among health care workers, NWR, Cameroon.
AUTHORS	Akazong, Etheline; Tume, Christopher; Ayong, Lawrence; Njouom, Richard; Kenmoe, Sebastien; Njankouo, Ripa; Kuate, Jules-Roger

VERSION 1 – REVIEW

REVIEWER	Komatsu, Haruki Toho University, Pediatrics
REVIEW RETURNED	09-Nov-2020

GENERAL COMMENTS	<p>The authors evaluated the HBV sero-status of healthcare workers (HCWs) in the North West region of Cameroon. This research shows that the prevalence of the exposure to HBV is high in the HCWs, but the majority of HCWs does not have a history of hepatitis B vaccines. This is a grave situation in the point of view of preventing HCWs from HBV infection.</p> <p>Major revisions</p> <ol style="list-style-type: none">1)The classification of sero-status is inappropriate and should be revised. Although HBeAg-positive people are defined to be "infective", HBsAg-positive/anti-HBe-positive people can transmit HBV to other persons.2) The detailed of sero-status should be added to Table 2.3) Was anti-HBe measured? Although anti-HBe is described in the methods section, there is no data about anti-HBe in the text. On the other hand, HBeAg assay is not described in the method section.4)It is surprising that the prevalence of HBV vaccination is low in young HCWs. I think that neonatal universal vaccination has already started in Cameroon. The authors should show the reason why the rate of HBV vaccination is low in young HCWs. Moreover, neonatal immunization program should be introduced.5)English is poor. It is indispensable to check this article by a negative English speaker. <p>Minor revisions</p> <ol style="list-style-type: none">1)"Hepatitis B infection" should be changed to " hepatitis B virus infection" in the introduction.2)WHO, HIV, HCV and CDC should be spelled out in the first appearance of the text.3)What are 8.75% and 10.6%? (page 4) Are the figures the
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	rate of HBsAg?
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REVIEWER	Teles, Sheila Universidade Federal de Goias
REVIEW RETURNED	21-Nov-2020

GENERAL COMMENTS	<p>Thank you for asking me to review this paper. I carefully read the manuscript, and I do not consider that this study provides any additional information on the epidemiology of HBV among Health Care Workers (HCWs) in Cameroon. In addition, there is an important overlap between this investigation and a paper recently published by the same research group (reference 8; BMJ Open. 2020. doi: 10.1136 / bmjopen-2019-031075).</p> <p>I strongly recommend the author review their "Case definition".</p> <p>Reading suggestion: Villar et al. Update on hepatitis B and C virus diagnosis. World J Virol 2015 November 12; 4(4): 323-342. DOI: 10.5501/wjv.v4.i4.323</p>
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REVIEWER	Genovese, Cristina University of Messina, BIOMORF
REVIEW RETURNED	23-Nov-2020

GENERAL COMMENTS	<p>the manuscript submitted treats a very interesting and current topic. However, some aspects should be addressed before to consider the paper suitable for potential publication.</p> <p>Please find below my recommendations:</p> <ul style="list-style-type: none"> - The abstract must be improved; in particular, the no information about the study period and sampling are present and, moreover, in background authors stated that the main route of transmission is contact with body fluid, please add also parenteral exposure; - Background must be improved: the authors must report the main schedule for immunization, the parenteral exposure route and the must give also an international background (add references of study in other country, revise the text by making changes that make the bibliographic research wider, more complete and international). - Results are well presented but their interpretation should be broadened both in the results section and in the discussions one. - Please add selection bias, Ascertainment bias in the result section and other bias in the limitation of the study - The sample was selected by all HCWS present in Bamenda Health District but the overall adherence is not reported (hoe many HCWS are present in the district?). Moreover, the sample size is represented by nurses for 56.7%. This is a limit of the study. - Multivariate analysis would be useful in statistical analysis to analyze confounding factors. - Discussion section must be improved according to indication of the reviewer
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VERSION 1 – AUTHOR RESPONSE

Reviewer 1: Haruki Komatsu		
4	The classification of sero-status is inappropriate and should be revised. Although HBeAg-positive people are defined to be “infective”, HBsAg-positive/anti-HBe-positive people can transmit HBV to other persons.	HBeAg is a serological marker that indicates the presence of HBV DNA in blood circulation in wild-type HBV. As the immune system clears HBV DNA, HBeAg disappears and anti-HBe appears. Mutations in rare cases can result in HBV DNA being present in blood circulation in the absence of HBeAg. Because there is no ELISA kit to determine the presence of HBV DNA in serum and the mutation is rare, we defined infectivity as the presence of HBsAg and absence of anti-HBe. This classification of infectivity is the best classification using ELISA kits but is a limitation to the study given that we don't test for HBV DNA in serum.
5	The detailed of sero-status should be added to Table 2.	We have no idea on the details to include. The table is a summary of the results obtained. The raw dataset is available in fig share: (https://doi.org/10.6084/m9.figshare.13503231.v1)
6	Was anti-HBe measured? Although anti-HBe is described in the methods section, there is no data about anti-HBe in the text. On the other hand, HBeAg assay is not described in the method section.	Anti-HBe was measured and used in determining infectivity. The raw data has been uploaded in fig share: (https://doi.org/10.6084/m9.figshare.13503231.v1). However, HBeAg was not measured
7	It is surprising that the prevalence of HBV vaccination is low in young HCWs. I think that neonatal universal vaccination has already started in Cameroon. The authors should show the reason why the rate of HBV vaccination is low in young HCWs. Moreover, neonatal immunization program should be introduced.	The HBV vaccine was included in the expanded immunization program administered at 6weeks, 10weeks and 14 weeks since 2004. Unfortunately, this vaccine cannot provide adequate protection in adulthood. This might justify the increase in susceptibility and decrease in infection rate in the (16-26) years age group.
8	English is poor. It is	This has been done

	indispensable to check this article by a native English speaker	
9	"Hepatitis B infection" should be changed to "hepatitis B virus infection" in the introduction	This has been corrected
10	WHO, HIV, HCV and CDC should be spelled out in the first appearance of the text	This has been corrected
11	What are 8.75% and 10.6%? (page 4) Are the figures the rate of HBsAg?	8.75% is the national prevalence of HBsAg among HCWs reported in a study published in 2018 while 10.6% is the rate of HBsAg among HCWs reported in a recent study.
<p>Reviewer Name: Sheila Araujo Teles</p>		
12	<p>I carefully read the manuscript, and I do not consider that this study provides any additional information on the epidemiology of HBV among Health Care Workers (HCWs) in Cameroon. In addition, there is an important overlap between this investigation and a paper recently published by the same research group (reference 8; BMJ Open. 2020. doi: 10.1136 / bmjopen-2019-031075). I strongly recommend the author review their "Case definition".</p> <p>Reading suggestion: Villar et al. Update on hepatitis B and C virus diagnosis. World J Virol 2015 November</p>	<p>We did not realise that the dataset had not been updated. The dataset has been updated (https://doi.org/10.6084/m9.figshare.13503231.v1).</p> <p>The overlap is in the sample population.</p> <p>'Case definition' was done following the CDC guideline (interpretation of Hepatitis B serologic test results) published in 2005. The case definition proposed by CDC in 2005 is very similar to the case definition proposed by WHO, 2017 (Guidelines on hepatitis B and C testing, P52). Thank you for recommending the paper (Villar et al, 2015).</p>

	12; 4(4): 323-342. DOI: 10.5501/wjv.v4.i4.323	
<p>Reviewer</p> <p>Name: Cristina</p> <p>Genovese</p>		
13	The abstract must be improved; in particular, the no information about the study period and sampling are present and, moreover, in background authors stated that the main route of transmission is contact with body fluid, please add also parenteral exposure	The abstract has been updated.
14	Background must be improved: the authors must report the main schedule for immunization, the parenteral exposure route and the must give also an international background (add references of study in other country, revise the text by making changes that make the bibliographic research wider, more complete and international)	The background has been edited.
15	Results are well presented but their interpretation should be broadened both in the results section and in the discussions one.	The results have been edited while focusing on the primary objective.
16	Please add selection bias, Ascertainment bias in the result section and other bias in the limitation of the study	Bias was minimized to the best of our ability and we are not aware of any bias which may stand out before the study, during the study or while interpreting data. Because we are aware of some limitations to this study, limitations to the study are listed in the limitation section.

17	The sample was selected by all HCWS present in Bamenda Health District but the overall adherence is not reported (hoe many HCWS are present in the district?). Moreover, the sample size is represented by nurses for 56.7%. This is a limit of the study.	Our target was 70% of HCWS present in our study area during the sampling period. Nurses represented 56.7% of our total study population.
18	Multivariate analysis would be useful in statistical analysis to analyse confounding factors	This has been done
19	Discussion section must be improved according to indication of the reviewer	This has been done
20	Table 2 must be improved: make it more readable	This has been done

VERSION 2 – REVIEW

REVIEWER	Komatsu, Haruki Toho University, Pediatrics
REVIEW RETURNED	11-Jan-2021

GENERAL COMMENTS	<p>Although this article is well revised, a few minor revisions are necessary.</p> <p>1. Readers want to know the background of HB vaccine policy in Cameroon. The other reviewer also suggests this point. 'The HBV vaccine was included in the expanded immunization program administered at 6weeks, 10weeks and 14 weeks since 2004` should be introduced.</p> <p>2`prevalence of HBV' should be changed to `prevalence of HBsAg positivity' in page 4.</p>
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VERSION 2 – AUTHOR RESPONSE

Reviewer Name: Dr. Haruki Komatsu		
2	Readers want to know the background of HB vaccine policy in Cameroon. The other reviewer also suggests this point. 'The HBV vaccine was included in the expanded	This has been

	immunization program administered at 6weeks, 10weeks and 14 weeks since 2004` should be introduced.	included
3	Prevalence of HBV` should be changed to `prevalence of HBsAg positivity` in page 4.	This has been edited

VERSION 3 – REVIEW

REVIEWER	Komatsu, Haruki Toho University, Pediatrics
REVIEW RETURNED	26-Mar-2021

GENERAL COMMENTS	This article is well revised.
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