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OPEN PEER REVIEW

Screening of Occult Hepatitis B and C Virus Infection in Working Children, Tehran, Iran

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

1 comment · 5 Nov 2021

Associate Editor

MINOR REVISION 5 Nov 2021

Dear author
Please provide a more complete explanation of the sampling process.
Regards

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear colleague,

I am writing to inform you that, I have submitted a revision of my Manuscript

Manuscript ID: 118763 with title: Occult HCV Infection, and Evaluation of Anemia, Calcium and Phosphate Levels between Working Children, Tehran, Iran. I have been answering to each of the reviewer comments point-by-point. I hope you accept my response.

Kind regards,

Farah Bokharaei-Salim

Response to Reviewers' Comments:

Reviewer 1:

Thank you for submission of Occult HCV Infection, and Evaluation of Anemia, Calcium and Phosphate Levels between Working Children, Tehran, Iran article.

1. This is a valuable study with many results, please arrange the information systematically and discuss them in the discussion part accordingly.

Reply: Thank you for your highly detailed consideration, and also thank you for taking the time to review my article and try to improve it. I have done as you proposed.

2. Abstract: The objective of study was check the anemia and HBV and HCV status in cases but there is no information about anemia and Ca status in the result

Reply: It was a very good suggestion. I analyzed hemoglobin and calcium in a categorized way and noticed the anemia in children and included it in the table. Thank you for your attention

3. Material and Method:

What is the ethical code of your study?

Reply: I added this sentence to my manuscript:

The current research was approved by the Iran University of Medical Sciences (IUMS), Tehran, Iran, in accordance with Helsinki Declaration (The ethical code: IR.IUMS.FMD.REC.1398.541),

4. Results:

The result part gives the HBV and HCV results of HIV Ag/Ab negative children. Was checking HIV status a part of your study?

Reply: Testing for HIV infection was not in my proposal, but I did it to complete my research, but because it was not in my plan, I did not include it in the title of the article.

5. Does the "a significant association was observed between gender and age." Means higher age was associated with male gender? This question can be answered for another variable. Some statistical relationship calculation is not rational for example relationship between nationality and WBC count.

Reply: This was the case in our statistical community. I put it in the article because I had the information. I can delete it if you think appropriate.

6. Can we have a reliable result of statistical evaluation with two positive HBsAg results?

Reply: In this study, I researched 370 working children and was able to find two children who were HBsAg positive. These two may be small, but you know working on 370 children and taking blood from them and planning for this project was very difficult. Anyway we could only find two people among the children and we might not even be able to find even one. I do not think that finding positive results in research does not diminish the value of research, and this is a valuable finding in itself.

7. Discussion:

Discussion is not well designed. There are a lot of results from different studies but there is not effective analysis of these results in comparison to this study. Plz give the results of studies that are similar with your situation there is no need to give information about HIV positive children. Plz give the results of other studies in your variables and discuss the differences and similarities.

Reply: I have done as you proposed.

8. Normal value of Ca and Phosphorus are not equal with normal body reservoir of these elements.

Reply: You are absolutely right, but there is no way to measure the amount of these elements in the body, we have to measure the amount in the blood and guess what the state of the body is in terms of these elements.

9. Author contribution: Plz don’t give the authors full name in this part.

Reply: It was done as you suggested.

Author’s contribution: A M, S G and F BS designed the study and were responsible for the overall research management. K K, R KE, F DD, R B, M S, H K, M E, and A F organized the analysis. A M, S G and F BS, and K K prepared the manuscript. It is noteworthy that all the authors contributed to the final version of this manuscript.

10. Plz check the need for total number column in your tables.

Reply: I think the existence of this column can show us the general situation at a glance and can be valuable, but if you need to delete it, let me delete it.

Response to Reviewers' Comments:

Reviewer 2:

1. It is suggested that the title of the article be more concise such as "screening of occult HCV and HBV Infection, in Working Children, Tehran, Iran".

Reply: I have done as you proposed, and changed the title of manuscript to:

Screening of Occult HCV and HBV Infection, in Working Children, Tehran, Iran

2. According to the purpose of the article, mentioning calcium, phosphorus, and anemia in the title of the article is not necessary.

Reply: With your suggestions, I changed the title to:

Screening of Occult HCV and HBV Infection, in Working Children, Tehran, Iran

3. How old was the participant with HBS-Ag and HCV? Because the majority of HBV and HCV infection in children is vertical and it is important in conclusion as a risk factor of infection in working children.

Reply: I made a table that gives complete information about the status of the laboratory results of the children in question and added it to the manuscript. I hope it is acceptable.

Table 3: Complete information about demographic, and laboratory information of the studied Working Children

No.	Age/ Gender	Nationality	ALT[3] (IU/L)	AST[4] (IU/L)	HCV -Ab	HCV-RNA in Plasma	HCV-gen[5] in plasma	HCV-RNA in PBMCs[6]	HCV-gen in PBMCs	HBs-Ag	HBs-Ab	HBc-Ab	HBe-Ag	HBe-Ab	HBV-DNA in plasma	HBV-DNA in PBMCs	Comments
166	10/M[1]	Afghan	23	25	–	–	–	–	–	+	+	–	–	–	–	–	–
113	12/M	Afghan	19	20	–	–	–	–	–	–	+	+	–	–	–	–	–
122	11/F[2]	Afghan	17	18	–	–	–	–	–	+	+	+	–	–	–	–	–
177	12/M	Iranian	15	14	–	–	–	–	–	–	–	+	–	–	–	–	Isolated HBcAb
283	15/M	Afghan	27	30	–	–	–	+	1a	–	–	–	–	–	–	–	OCI[7]

1. Male 2. Female 3. Alanine aminotransferase
4. Aspartate amino transferase 5. Genotype 6. Peripheral blood mononuclear cell (PBMCs)
7. Occult HCV infection

4. In participants who were positive HBS-Ag, has HBe -Ag been checked to rule out laboratory error? Given that the presence of HBe -Ag in the serum indicates the replication phase of the virus and HBV PCR is expected.

Reply: We performed this test to rule out laboratory errors, and the results were given in Table 3, which we just created.

Associate Editor's Comments:

Associate Editor 1:

Please provide a more complete explanation of the sampling process.

Reply: Collection of the participant's samples is written exactly and completely, and I do not know what to enter. Please advice.

Associate Editor 2:

Your manuscript has now passed through the review stage and is ready for revision.

Reply: Thank you

Editorial comments

To ensure the Editor and Reviewers will be able to recommend that your revised manuscript is accepted, please pay careful attention to each of the comments that have

been pasted underneath this email. This way we can avoid future rounds of clarifications and revisions, moving swiftly to a decision.

1. Please provide a point-by-point response to the comments

2. Please highlight all the amends on your manuscript

3. Use line numbering and page number in the next submission

4. English language is weak and should be improved

Reply: Thank you for your highly detailed consideration, and also thank you for taking the time to review my article and try to improve it. I have done as you proposed.

This manuscript has been edited by Kowsar Institute on the date of 1399-12-29 with 1284228 number.

Other shortcomings

The abstract, the result section should be improved with the patients' characteristics (Male/female ratio, mean age±SD, ethnicity proportion, ...)

Reply: I have done as you proposed.

Methods: From February 2018 to May 2019, this cross-sectional research was performed on 370 Iranian and Afghan working children. HBsAg, HBsAb, HBcAb, and also anti-HCV Ab, were evaluated using the ELISA. Furthermore, HCV-RNA and genomic HBV-DNA in the plasma and PBMC specimens of studied participants were investigated. RFLP method was used to determine the genotype of HCV and sequencing was performed to confirm.

Results: The mean age of the participants was 10.1 ± 2.1 years (range 6-15 years), and 229 (61.9%) were male. None of the studied children had any detectable HBV-DNA in the plasma and PBMC. The HCV genome was not detected in the plasma of the children, but HCV-RNA was detected in the PBMC sample of one child (0.3%). Therefore, one of the children had occult HCV infection (OCI). The genotype of HCV in this child was subtype 1a. Furthermore, HBsAb was detected in the Iranian (41.5%), and Afghan children (40.0%), and two (0.54%) of the working children were HBsAg positive. In 3 participants (0.8%), a positive HBcAb test result was noted.

Correct keywords:

"Hepatitis B virus (HBV), Hepatitis C virus (HCV), Working children, Tehran, Iran"

Reply: I have done as you proposed.

Remove "Objectives" and its' subheading.

Reply: I have done as you proposed.

Add "inclusion and exclusion" criteria to the "Materials and Methods".

Reply: I have done as you proposed.

Discussion should be started with overall study findings.

Reply: I have done as you proposed.

Add study limitation at the end of the discussion section.

Reply: I added this part to the discussion:

A limitation in the present study was that some parents of the studied children were not interested in their children entering this study and because of this they did not enter the present study. During the blood sampling of working children, some of them did not cooperate and did not allow blood sampling, so they were not included in the current survey.

The conclusion section should be revised (remove "(0.3%)". Improve the English language. Rewrite the following statements with better words

"The results of this research demonstrated that none of the working children were HCVRNA-/HBV-DNA-positive synchronously. But it is noteworthy that in these children with very low prevalence (0.3%), occult HCV infection exist.")

Reply: I omitted 0.3%, and I added this part to the conclusion:

The findings of the current survey demonstrated that none of the studied children were HCV-RNA-/HBV-DNA-positive synchronously. But it is noteworthy that in these children with very low prevalence, occult HCV infection exist. Therefore, it seems that in addition to the routine experiments to detect different infectious diseases in this population, appropriate tests to diagnose OCI are informative and should be considered.

2 Revision 1

0 comments

No public comments in this round.

3

Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Journal: Archives of Pediatric Infectious Diseases

Manuscript ID: 118763

Manuscript Title: Screening of Occult HCV and HBV Infection, in Working Children, Tehran, Iran

Revision: 1

Dear colleague,

I am writing to inform you that, I have submitted a revision of my Manuscript.

Manuscript ID: 118763 with title Revision [1]: **‘’Screening of Occult HCV and HBV Infection, in Working Children, Tehran, Iran ‘’**. I have been answering to each of the reviewer comments point-by-point. I hope you accept my response.

Kind regards,

Farah Bokharaei-Salim

> Reviewers' Comments:

> Associate Editor's Comments:

First of all, from the point of view of the language, English is quite poor and should be extensively revised. The manuscript's English language is not acceptable in its current form (many parts are difficult to understand).

Reply: This article was sent to Kowsar Publications for editing and was reviewed and changed. I hope it is acceptable. Modified areas were changed color.

2. Line 189: replace "viral infections" with "HBV and HCV infections"

Reply: I have done as you proposed, and changed the color to red.

3. Readers may be confused by these two statements: Line 195 "Thus, studied children were negative for hepatitis B virus infection and OBI." and lines 201-202 "In addition, totally, 2 (0.54%) test results were observed for HBsAg detection in both Iranian and Afghan participants." Remove both of them and rewrite them with better words.

Reply:

When we cannot detect HBV DNA in plasma of people, this person doesn't have active HBV infection, and when we cannot detect HBV DNA in plasma and PBMC of the people, this person doesn't have OBI.

First sentence changed to:

Thus, studied children were negative for active hepatitis B virus infection and for occult HBV infection. Furthermore, none of the working children had any detectable HCV-RNA in plasma. It is noteworthy that, 1 (0.3%) of these studied children had detectable HCV-RNA in the PBMC specimen. Therefore, one of the Afghan children had OCI, and he was infected with HCV genotype 1a.

Negative test results were reported for HCV Abs detection in both the Iranian and Afghan populations. In addition, two Afghan children were positive for HBsAg. Therefore, the percentage of HBV infection in these children is (0.54%).

3. Also, considering four positive HBcAb results, more attention is necessary for final conclusion. HBcAb should be defined (total versus IgM serum level). HBcAb could be the sole HBV marker during acute HBV infection (window period). So, it seems that you find four HBV infections in the studied cases.

Reply: In this study we find 3 (0.8%) children for HBcAb. In one of them only HBcAb was positive. This child may be in the window period, but his HBeAb is negative, and this person

may be Isolated HBcAb positive, and she has been infected with hepatitis B for a long time ago and now is only positive for HBcAb.

In general, because this study was designed to detect occult HBV and HCV, discussion of each item is very difficult and long.

Therefore, this part was added to the article.

In addition, a positive HBcAb test result was detected in three participants. Out of three (0.8%) positive HBcAb participants, two (0.9%) and one (0.7%) participants were male and female, respectively. Thus, it appears that 0.8% of children may have been exposed to the hepatitis virus infection during their lifetime.

4. Line 215: why did you consider "Hb=11.5" for identifying anaemia? Add reference.

Reply: I added this reference to my manuscript (23)

23. Akbarpour E, Paridar Y, Mohammadi Z, Mard A, Danehchin L, Abolnezhadian F, et al. Anemia prevalence, severity, types, and correlates among adult women and men in a multiethnic Iranian population: the Khuzestan Comprehensive Health Study (KCHS). BMC Public Health. 2022;22(1):168.

5. Line 218: why did you consider "Ca=8.8" for identifying hypocalcemia? Add reference.

Reply: I added this reference to my manuscript (4)

4. Vannucci L, Fossi C, Quattrini S, Guasti L, Pampaloni B, Gronchi G, et al. Calcium Intake in Bone Health: A Focus on Calcium-Rich Mineral Waters. Nutrients. 2018;10(12).

6. Lines 216-217: "Low haemoglobin and Iron levels in these participants lead to anaemia (22)." This statement is not meaningful. Remove it.

Reply:

I removed this sentence and its reference (22)

[Low haemoglobin and Iron levels in these participants lead to anaemia (22)].

The hemoglobin level was classified as below and above 11.5 and it was observed that the hemoglobin level in women is much lower than men and it seems that women suffer from anemia (23). Due to anemia, it seems that these children should be treated for anemia. Also the level of calcium was classified as below and above 8. 8 (4), and it was observed that calcium levels in men are lower than women and men seem to suffer from relative calcium deficiency than women.

7. Lines 217-219 are written in very poor English language.

Reply: I have done as you proposed, and changed the color to red.

8. Line 247-248: "The values of the present study were considerably less than some previous studies conducted in Iran", this statement is not meaningful.

Reply: This sentence was removed due to the presence of the previous sentence.

3 Revision 2

0 comments

No public comments in this round.