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OPEN PEER REVIEW

Helicobacter pylori Infection and Its Association with Mediterranean Diet Adherence in Lebanese Children and Adolescents: A Cross-sectional Study

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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

2 comments · 16 Apr 2024 – 10 May 2024

Referee 1 Reviewer

MAJOR REVISION 16 Apr 2024

Thanks for this review invitation.
There are a few points that should be considered in this manuscript.
1. The title is not indicative of their study policy.

2. How did they estimate the family income? The term “sufficient” is general.
3. What is the relationship between income and this kind of feeding? Eating unwashed vegetables, etc., is a cultural factor and is not directly related to their income.
4. What is the main concept of this study?
5. MD, H. pylori infection, and income are 3 factors with many confounding factors related to false positives or false negatives.

Associate Editor

MAJOR REVISION 10 May 2024

Reviewer 1:
Dear authors, please consider the following comments:
Comment 1: In the results section, you stated that " bivariate analysis has shown ...". What do you mean by " bivariate analysis"? You did a univariate analysis.
Comment 2: In the results section, you stated that " bivariate analysis has shown that H.pylori infection did not exhibit any significant differences across age, ... ($p<0.05$)". You should change the value inside the parentheses to $P>0.05$ to show nonsignificant variables.
Comment 3: In the results section, the p-value you reported for a relationship between H.pylori infection and infrequent washing of fruits and vegetables in Table 1 does not coincide with the value you reported in the text.
Comment 4: In Table 2, you didn't mark the p-value for "dairy for breakfast" with a sign. Please add it.
Comment 5: Using " multiple binary logistic regression" instead of " multivariate binary logistic regression" is better.

Reviewer 2:
Thanks for this review invitation.
A few points should be considered in this manuscript.
1. The title is not indicative of their study policy.
2. How did they estimate the family income? Sufficient is a general term.
3. What is the relationship between income and this kind of feeding? Eating unwashed vegetables, etc., is a cultural factor and is not directly related to their income.
4. What is the main concept of this study?
5. MD, H. pylori infection, and income are 3 factors with many false-positive- or false-negative-related confounding factors.

Reviewer 3:
Dear Authors
I studied your manuscript carefully and offer the following suggestions:
1- Study design and data collection
“A cross-sectional study was carried out between June 2023 and November 2023. A total of 290 children and

adolescents aged between 2 years and 18 years visiting the pediatric gastroenterologist department of two hospitals located in a suburban area in Northern Lebanon were enrolled. Among them, 198 participants met the eligibility criteria and were included in this study (Figure 1). " Kindly mention these data in the results section.

2- Results

"The sample consisted of 198 children and adolescents (51.5% male and 48.5% female). The average age of the participants was 4.52 [2-18]. " Please mention the SD (standard deviation).

3- Discussion

"Lebanon's current economic crisis dating since 2019 was described as one of the three worst events in the world since the middle of the nineteenth century, according to the World Bank report (22). The value of the Lebanese Pound dropped dramatically and it was coupled with unstable finances, which have taken a toll on the quality of life parameters in Lebanon. Access to food has become increasingly difficult due to the minimal financial power of the population. In addition, the paucity of household finances has exacerbated the access to basic health services such as accurate and affordable diagnosis of diseases including infectious diseases. All these factors highlight the severity of the current situation and the need for further assessments and strategies to promote health and well-being. So, we designed this cross-sectional study to assess the adherence to MD during the economic crisis in the young Lebanese population and its association with H. pylori infection. " This paragraph should be mentioned in the "Introduction" section.

4- "H. pylori was detected in 12.1% of children and adolescents." I suggest you compare this result with the results of other studies that use the same method (Stool H. pylori Ag Test).

5- Conclusion

In the conclusion section, it is better to state the general conclusion drawn from the discussion section. It is not necessary to mention the numerical data from the results section or to repeat the sentences of the discussion or results section. Please revise and shorten the conclusion by observing these points.

Thank you.

Reviewer 4:

Dear authors, I studied your manuscript with interest. Please consider the following comments:

1. Regarding the transmission of Helicobacter infection through the fecal-oral route, are you considering intervening factors such as kissing, using a shared water glass or other shared equipment, and consuming hand-sold food?

2. How did they estimate the family income? Sufficient income is a general term.

3. English grammar needs to be revised. Please revise and shorten the conclusion.

4. The title is not indicative of their study policy. Please revise.

sincerely you

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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.

جامعة بيروت العربية
BEIRUT ARAB UNIVERSITY

Dear Editor of *Archives of Pediatric Infectious Diseases*,

We thank you for serving as editor for our manuscript and for selecting knowledgeable reviewers.

We are pleased that all reviewers found our manuscript informative and interesting and we thank you and the reviewers for thoughtful reading, suggestions, and highly constructive comments.

We have addressed the concerns in a point-by-point manner and have accordingly revised the manuscript which turned out to be more intelligible and coherent. We have attached our responses (in blue) in the response letter as well as in the revised manuscript (in yellow).

We hope you find the revised manuscript suitable for publication in the *Archives of Pediatric Infectious Diseases*.

Please feel free to contact us if you have any further questions.

Thank you very much for your consideration.

Reviewer 1

Dear Authors

I studied your manuscript carefully and the below suggestions will be offer:

1- Study design and data collection

“A cross-sectional study was carried out between June 2023 and November 2023. A total of 290 children and adolescents aged between 2 years and 18 years visiting the pediatric gastroenterologist department of two hospitals located in a suburban area in Northern Lebanon were enrolled. Among them, 198 participants met the eligibility criteria and were included in this study (Figure 1). “Kindly, mention these data at result section.

REPLY: We would like to thank you for your suggestions. The paragraph was moved to the results section according to demands.

2- Results

“The sample consisted of 198 children and adolescents (51.5% male and 48.5% female). The average age of the participants was 4.52 [2-18]. “Please mention SD (standard deviation)

REPLY: The reviewer is correct. SD (standard deviation) was added.

3- Discussion

“Lebanon's current economic crises dating since 2019 was described as one of the three worst events in the world since the middle of the nineteenth century, according to the World Bank report (22). The value of the Lebanese Pound dropped dramatically and it was coupled with unstable finances, which have taken a toll on the quality of life parameters in Lebanon. Access to food has become increasingly difficult due to the minimal financial power of the population. In addition, the paucity of household finances has exacerbated the access to basic health services such as accurate and affordable diagnosis of diseases including infectious diseases. All these factors highlight the severity of the current situation and the need for further assessments and strategies to promote health and wellbeing. So, we designed this cross-sectional study to assess the adherence to MD during the economic crisis in the young Lebanese population and its association with H. pylori infection. “This paragraph should be mentioned at” Introduction” section.

REPLY: We agree with this suggestion. This paragraph was merged with the related paragraph in the introduction of the revised version as follows: *“Lebanon has been struggling since 2019 with an unwavering economic crisis that has dramatically expanded leading to increased rates of unemployment, inflation, and poverty (18, 19). The purchasing power of the Lebanese pound has decreased by more than 90%. In addition, the paucity of household finances has exacerbated the access to food and basic health services such as accurate and affordable diagnosis of diseases including infectious diseases (18). All these factors highlight the severity of the current situation and the need for further assessments and strategies to promote health and well-being.”*

4- “H. pylori was detected in 12.1% of children and adolescents.” I suggest you to compare this result with the results of other studies that use the same method (Stool H.pylori Ag Test)

The decent note was taken into consideration, and modifications were adopted as follows: *“Lower prevalence has been documented in Japan (3.7%) (22). However, reports from Iran (64.2%) and African countries, including Uganda (24.3%), Cameroon (52.27%), and Egypt (64.6%), have shown a higher prevalence of H. pylori infection in children (23-26). These discrepant findings could be attributed to poor sanitation and untreated water supplies (27).”*

5- Conclusion

In the conclusion section, it is better to state the general conclusion that is taken from the discussion section. It is not necessary to mention the data of the results section with numbers and to repeat the sentences of the discussion or results section. Please revise and shorten the conclusion part by observing these points.

REPLY: We complied with the request, and the passage was modified accordingly: *“This study showed a significant correlation between H. pylori infection and consumption of olive oil and dairy products. Therefore, longitudinal studies examining nutritional knowledge and food security are essential to provide insights into dietary factors associated with poor adherence to the MD and H. pylori infection. Furthermore, studies on the antimicrobial properties of natural products against H. pylori may lead to novel approaches for antibiotic-resistant strains in clinical practice.”*

Thank you.

Reviewer 2

Thanks for this review invitation.

There are few points that should be considered in this manuscript.

1. The title is not indicative of their study policy.

REPLY: The authors agreed with the reviewer’s comment and the title has been changed to be more indicative of the study policy as follows: *“Helicobacter pylori Infection and Its Association with Mediterranean Diet Adherence in Lebanese Children and Adolescents: A Cross-sectional Study”*

2. How did they estimate the family income? sufficient is a general term.

REPLY: Due to the economic crisis, the value of the Lebanese currency dropped, significantly impacting the entire economy. Inflation fluctuates, and the official minimum wage has decreased by 84%. Researchers in Lebanon are adopting a dichotomous scale with two levels, "sufficient" and "not sufficient," to reflect family income levels. Although this approach is general, it yields more reliable answers.

3. What is the relationship between income and this kind of feeding? Eating non washed vegetables or etc. is a cultural factor and does not directly related to their income.

REPLY: We aimed to investigate the association between washing vegetables and *H. pylori* infection to support the hypothesis that food can play a vital role in the transmission of the *H. pylori*. This finding was discussed in the following passage: *“This corroborates the hypothesis addressed by some authors considering H. pylori as a foodborne pathogen (28, 29).”.* Income was not included in this association.

4. What is the main concept of this study?

REPLY: The primary objective of this study is to explore the potential association between alterations in the Mediterranean diet, influenced by the economic crisis, and the frequency of *H. pylori* infection in Lebanon.

5. The MD and H. pylori infection and income are 3 factors with many false positive or negative related confounding factors.

REPLY: The primary objective of this study was to investigate the association between adherence to the Mediterranean diet and *Helicobacter pylori* infection (as a dependent variable). A secondary objective was to assess the association of the infection with patients' characteristics. In our study, we first examined overall adherence to the Mediterranean diet alongside the items included in the Mediterranean diet score questionnaire, to assess any possible association with *Helicobacter pylori* infection. Second, based on a literature review and to the best of our knowledge, most confounding variables, such as age and gender, were included in the bivariate analysis and did not show significant associations. Furthermore, multiple logistic regression was used to finalize the results. The results ultimately presented significant associations.

Reviewer 3

Dear authors, please consider below comments:

Comment 1: In results section, you stated that " bivariate analysis has shown ...", what do you mean by " bivariate analysis", you did univariate analysis.

REPLY: The primary objective of this study was to investigate the association between adherence to the Mediterranean diet and *Helicobacter pylori* infection. In this perspective, a bivariate analysis was performed to investigate this relationship.

Comment 2: In results section, you stated that " bivariate analysis has shown that H. pylori infection did not exhibit any significant differences across age, ... ($p<0.05$)", you should change the value inside the parentheses to $P>0.05$, to show nonsignificant variables.

REPLY: We apologize for this inaccuracy and thank the reviewer for detecting it. The value was modified accordingly.

Comment 3: In results section, the p-value that you reported for relation between H. pylori infection and infrequent washing of fruits and vegetables in table 1 is not coincide with the value that you reported in the text.

REPLY: The value was modified accordingly.

Comment 4: In table 2, you didn't mark p value for "dairy for breakfast" with a sign, please add it.

REPLY: The sign “*” was added.

Comment 5: it is better that you used " multiple binary logistic regression" instead of " multivariate binary logistic regression".

REPLY: We are sorry for not using the right term. The latter was substituted with *“multiple binary logistic regression”*.

Reviewer 4

Dear authors, I studied your manuscript with interest please consider the following comments:

1. Regarding the route of transmission of Helicobacter infection through fecal-oral are you considering or not the intervening factors such as kissing, using a common glass water, or other shared equipment, and consuming food from hand-sold?

REPLY: Thank you for your insightful comments. In the current study, we focused primarily on identifying associations between the Mediterranean diet (MD) and *H. pylori* infection and did not extensively investigate the fecal-oral transmission route. However, we are currently conducting a related study where we are examining the potential transmission of *H. pylori* through the communal use of shisha equipment, a popular smoking practice in Arab countries where users share the same smoking tools by mouth. This investigation aims to further our understanding of transmission pathways alongside dietary influences.

2. How did they estimate the family income? Sufficient income is a general term.

REPLY: Due to the economic crisis, the value of the Lebanese currency dropped, significantly impacting the entire economy. Inflation fluctuates, and the official minimum wage has decreased by 84%. Researchers in Lebanon are adopting a dichotomous scale with two levels, "sufficient" and "not sufficient," to reflect family income levels. Although this approach is general, it yields more reliable answers.

3. English grammar needs to be revised. Please revise and shorten the conclusion part.

REPLY: English grammar was revised and the conclusion was shortened as follows: "*This study showed a significant correlation between H. pylori infection and consumption of olive oil and dairy products. Therefore, longitudinal studies examining nutritional knowledge and food security are essential to provide insights into dietary factors associated with poor adherence to the MD and H. pylori infection. Furthermore, studies on the antimicrobial properties of natural products against H. pylori may lead to novel approaches for antibiotic-resistant strains in clinical practice*."

4. The title is not indicative of their study policy. pls, revise.

REPLY: The title has been changed to be more indicative of the study policy.as follows: *"Helicobacter pylori Infection and Its Association with Mediterranean Diet Adherence in Lebanese Children and Adolescents: A Cross-sectional Study"*

2 Revision 1

2 comments · 16 Aug 2024 – 30 Aug 2024

Referee 1 Reviewer

ACCEPT 16 Aug 2024

Thanks for this invitation.
The mentioned points have been revised completely.

Peiman Nasri Reviewer

ACCEPT 30 Aug 2024

Dear authors, thank you for applying my suggestions to your manuscript.

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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.

جامعة بيروت العربية
BEIRUT ARAB UNIVERSITY

Dear Editor of *Archives of Pediatric Infectious Diseases*,

We thank you for serving as editor for our manuscript and for selecting knowledgeable reviewers.

We are pleased that all reviewers found our manuscript informative and interesting and we thank you and the reviewers for thoughtful reading, suggestions, and highly constructive comments.

We have addressed the concerns in a point-by-point manner and have accordingly revised the manuscript which turned out to be more intelligible and coherent. We have attached our responses (in blue) in the response letter as well as in the revised manuscript (in yellow).

We hope you find the revised manuscript suitable for publication in the *Archives of Pediatric Infectious Diseases*.

Please feel free to contact us if you have any further questions.

Thank you very much for your consideration.

Reviewer 1

Thanks for this invitation.

The mentioned points have been revised completely.

Reviewer 2

Dear authors, thank you for applying my suggestions to your manuscript.

Reviewer 3

Dear authors, thanks for applying my comments, there are few points that should be considered:

Comment 1: you entered " Washing fruits & vegetables before eating" variable in multiple binary logistic regression, but you didn't univariate analysis for it and you didn't report any information for this variable in table 2. Please add it to other tables.

REPLY: Thank you for your comments. "Washing fruits & vegetables before eating" variable was added in the Table 1. However, we only included the 16

items of the Mediterranean diet (MD) in the Table 2. “Washing fruits & vegetables before eating” is not an item of the MD, for this reason it was not included.

Comment 2: you entered three variables include: Washing fruits & vegetables before eating, Olive oil, Dairy for breakfast. How did you choose these variables for multiple model? Please explain about it.

REPLY: We complied with the request, and the passage was modified accordingly in the results section (highlighted in yellow): *“A multiple binary logistic regression analysis was conducted for the factors that showed signification association with H. pylori infection in the bivariate analysis: washing fruits and vegetables before eating, and consumption of olive oil and dairy products.”*

Associate Editor 1

Dear authors, thanks for applying my comments,

There are a few points that should be considered:

Comment 1: you entered the “ Washing fruits & vegetables before eating” variable in multiple binary logistic regression, but you didn’t do univariate analysis for it and you didn’t report any information for this variable in Table 2. Please add it to other tables.

REPLY: Thank you for your comments. “Washing fruits & vegetables before eating” variable was added in the Table 1. However, we only included the 16 items of the Mediterranean diet (MD) in the Table 2. “Washing fruits & vegetables before eating” is not an item of the MD, for this reason it was not included.

Comment 2: you entered three variables including: Washing fruits & vegetables before eating, Olive oil, and Dairy for breakfast. How did you choose these variables for multiple models? Please explain about it.

REPLY: We complied with the request, and the passage was modified accordingly in the results section (highlighted in yellow): *“A multiple binary logistic regression analysis was conducted for the factors that showed signification association with H. pylori infection in the bivariate analysis: washing fruits and vegetables before eating, and consumption of olive oil and dairy products.”*

3 Revision 2

0 comments

No public comments in this round.