PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Factors affecting anaemia among women of reproductive age in Nepal: a multilevel and spatial analysis
AUTHORS	Sunuwar, Dev Ram; Singh, Devendra Raj; Adhikari, Bipin; Shrestha, Santosh; Pradhan, Pranil

VERSION 1 – REVIEW

REVIEWER	Abhishek Agarwal The INCLEN Trust International
REVIEW RETURNED	20-Sep-2020

GENERAL COMMENTS	The present article require following changes: Technical: a. Role of hormonal contraceptives is not clear (table and Text do not match) b. The present study reflects the demographic variations between the different geographical areas which has association with anemia, so nothing new to be learn from the study. Grammatical a. The spelling of anaemia or anemia are different at some places. b. There is a need to rephrase the line 76 - 80 as the rationale and objective is not clearly reflected. The reviewer provided a marked copy with additional comments. Please contact the publisher for full details.

REVIEWER	Dieudonne Hakizimana University of Global Health Equity (UGHE), Rwanda
REVIEW RETURNED	21-Oct-2020

GENERAL COMMENTS	The authors are addressing an important public health problem. The manuscript is well written but still needs improvement. Factors affecting anemia among women of reproductive age in Nepal: a multilevel and spatial analysis Reviewer: Dieudonne Hakizimana October 2020 General: the authors need to be consistent: either use anemia or anaemia (please revise the whole document). Abstract: Well written and clear. In the conclusion, multipronged approaches are not specific, the authors should consider using a clear term.

	Strengths and limitations of this study: It is better the author mention also other qualitative factors not collected in DHS were not included in the study. Background: P5 line 56. For clarity, authors can separate the paragraph and mention the country first [in Nepal, …]. It gives the impression that it is a continuation of the previous information. P6 line 76: the paragraph discussed the uniqueness of the study including using spatial analysis, identify factors associated with anemia using cluster sampling of nationally representative data. Some of the arguments are not correct. There are many studies that explored the factors associated with anemia in Nepal using the DHS data with national representation and collected using cluster sampling (the same data used in this study). Here are some examples: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6561639/ https://onlinelibrary.wiley.com/doi/full/10.1111/mcn.13044 https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0236449 The authors should discuss other studies that used the same data and justify what is unique in this study. Probably showing geographic variation with spatial analysis and why it is important. Moreover, the study does not show the factors influencing anemia by geographic region as it claims here. The study just describes the prevalence of anemia by geographic region. The results show the factors at the national level as it is in other studies. The author should justify why this study is important compared to the other mentioned above as they are using the same data. Method The author should give a description of the study setting for a better understanding of the context and the situation in the country. PAGE 6 Line 89: Not sure if the ERA is an abbreviation. If it is, it is used for the first time and should be written in full. Pa7 line 100 -103. The authors stated: .. women with available data on anemia…. were eligible for the survey. It is not clear if the author is describing the normal DHS sampling procedures as shown in figure 1 or the individuals included in the analysis for this study. The anemia is tested on a subset of the selected women. Women are not included in the study based on anemia data availability. The author should clarify if here they are describing the inclusion criteria for their analysis of the DHS sampling procedure and ensure they describe clearly. Moreover, Figure 1 describes the DHS data collection procedure for anemia. It is not adding much information as this study did not collect the data. The author should use the figure to describe their

	procedures in including individuals available in DHS dataset in their analysis if they excluded any and the exclusion criteria rather than describing the DHS procedure in the figure. P8 line 133: the authors mention: the mean value was used as a cut-off point of the proportion values for the categorization of community-level variables. The authors need to specify that it is only for the variables they calculated as it is not applicable to the province, residence. The use of the mean as the cut off for community female education and community wealth index should be justified. The cut off used. influence the findings. Was the decision of using the mean an expert opinion or there is a standard? If the authors are comparing people below the mean and above the mean, it is likely that those below the mean will be likely different from those above. The use of mean as cut off should be justified with evidences. Page 9 line 142. The sentence: “Data were adjusted for enumeration areas (EAs) and disproportionate sampling and non-response” is not clear. If the authors would like to mention they adjusted for the effects of the stratification and cluster sampling approaches used in DHS, they should explicitly mention that. It is not clear how enumeration areas and non-response-response were adjusted in this study. DHS researchers have already taken care of that in calculating the survey weights. In the results, the authors mention using the Pearson Chi-Square test for categorical variables and independent t-test for continuous variables, but this is not mentioned in the analysis section. Spatial analysis I am not very comfortable with Spatial statistical analysis; the editor should make sure they were appropriately used. In the analysis, the author talked about calculating the standardized prevalence ratio. They should describe in details how they calculated the prevalence ratio to help readers who will want to replicate the same study. S1 Table Plan for data coding and description of the study variables For recoding the current contraceptive use variable, the authors separated the not using with natural/barrier and permanent methods. There should be a justification for this. Physiologically, the two are not different in terms of the likelihood of having anemia. Minimum dietary diversity for women (MDD-W): Better to say met or not met Province: There is a typo in 1=Provice Why malaria-related variables were not included in the analysis while they are known to be among important risk factors for anemia? The authors are recommended to include these in the analysis. Results

	Page 11 line 201: typo: missing “were” More than one third (38.1%) of the participants…. Page 12 line 215: “the higher cases of anemia” should use prevalence instead of cases. Page 12 line 216: add “among women”: The prevalence of anemia was more “among women” who… The authors should be consistent when presenting the results. In some places, they are presenting percentages and the odds in others. Page 13 line 250 – 245: Women who belonged to communities with a high percentage of wealthy households had 1.48 times higher (aOR=1.48, 95% CI: 1.21-1.80) odds of anemia compared to those coming from a low percentage of the wealthy household; and women residing in communities with a high percentage of community female education had 1.39 times higher (aOR=1.39, 95% CI: 1.15-1.68) odds of anemia compared to those coming from the communities with a low percentage of education. The information presented here is different from the results in table 2. It is the other way around. This is very key for this study. You should revise. Table 1: Severe anemia, Moderate anemia, and Mild anemia should be in the prevalence of anemia column. For the Hemoglobin level, mean (+SD), there is a p-value, but it is not clear what was being tested. Did the author test the mean between the anemic and non-anemic? If it is the case, the mean/SD for non-anemic should also be reported. Some of the provinces are named Province-1, Province-2, and Province-5. The author should use the province names if they are available. The country context would help to clarify that. Some individuals were not included in the analysis for some variables. The N for 6,414 but for BMI (n=6411) and Source of drinking water (n=6084). Can the author provide justification? Discussion The subtitle “Overall findings” should be removed. It is expected that you discuss all findings. It is not clear what the subtitle means here. The discussion starts well with reminding the main finding. The authors are recommended to replace “serious” with “important” public health problem. Serious seems to be informal in public health practice. Page 15 line 289: the authors mention one of the reasons for the high prevalence of anemia in the Terai region is a possibility that WRA from the Terai region and high mountainous regions are more likely to be of a lower socioeconomic status and thus can afford less diversified diet compared to other provinces and districts. This is contrary to the findings of this study and other discussion arguments. The authors should revise the justification. In in this

	study, the middle-class families are at high risk of anemia compared to the poor class and MDD-W was not found to be a predicting factor. Moreover, in the discussion, the authors also mentioned that most of the Nepalese people consume iron-rich staple foods including cereal, grains, lentils, and animal source food regardless of wealth status. The authors also discuss malaria as one of the factors for anemia. It is not clear why the author did not include malaria-related variables in the analysis while they are collected in the DHS. P16 line 317: corroborate may not be an appropriate term – consider revising and use common terms like “similar findings”. P16 line 327: In this study, the prevalence of anemia was 32.3% in the poorest, 41.5% in poorer, 48.9% in middle, 43.4% in richer, and 35.9% in richest households. This should be in the results. It is not necessary to repeat the results in the discussion, just explain the results. P16 line 333: this sentence challenges your study: “Future research is critical to explore the association of household economic status and anemia among WRA in Nepal.”. Economic status was studied here and adjusted in all models. Does it mean the authors don’t trust the study results and recommend studying it again? The arguments about why the women in the middle category are more likely to have anemia compared to the poorest are not clear and convincing. They need to be supplemented with major differences between those categories. The authors said most of the Nepalese people [including middle and poor] consume iron-rich staple foods including cereal, grains, lentils, and animal source food regardless of wealth status. Thus, they should have similar risks, which is not the case in this study. P17 line 338: Relatively higher prevalence of anemia at a younger age could be because of lower dietary iron intake and the additional demand for iron to compensate for iron loss during menstruation. This contradicts the previous argument. Here you mention young people have lower dietary iron intake while in the previous paragraph you mentioned: most of the Nepalese people consume iron-rich staple foods including cereal, grains, lentils, and animal source food regardless of wealth status. The authors should make sure the arguments explaining the results are consistent. P 18 line 343: consider revising the language: In this study, the use of hormonal contraceptive methods was less likely to be associated with anemia among WRA. It should be those using hormonal contraceptive were less like likely to be anemic or had lower odds of anemia. P 18 line 360: could be due to the fact that WRA from Province-2 are more likely to be of a lower socioeconomic status and are less likely to afford a diverse diet. This argument contracts the study findings. Those poorer are less likely to be anemic compared to the middle and MDD-W was not a predicting factor to explain the differences. The authors should supplement the justifications. P18 line 44: The authors should support this argument with evidence: “with increase knowledge, women may also reduce the

	intake of tea, coffee, and some spices which are known to inhibit iron absorption". This argument is weak. Iron absorption is not the single risk factor for anemia. Moreover, you should also justify if communities with high tea, coffee, and spices consumption are at high risk of anemia. General comments on the discussion: The authors discuss many factors that may explain variations in anemia prevalence and risk. However, the authors do not compare and contradict the results with other studies in other settings. Moreover, it is not clear if the factors discussed in explaining the findings are particularly prone in the discussed regions compared to other regions. The authors should mention/justify that and make a comparison. For example, if the authors say: the majority (90%) of the population from the Terai region rely on groundwater especially shallow tube well for domestic purposes including drinking compared to XXX in the other region. Another example is Higher arsenic concentration can inhibit haem iron metabolism and increase erythrocyte hemolysis. Yes, that is known but we don't know how prevalent the condition in the region is compared to others, to be a possible explanation of anemia differences. Those are is just examples I picked from the discussion. The authors should revise their discussion and make comparisons throughout the discussion. Additionally, the authors should discuss the implications in terms of interventions in addressing anemia. For example, those with no education are at risk of anemia. And then what? How policy makers should use that information from the study? Which interventions should be put in place to address that considering the study findings? Strengths and limitation Page 19 line 372: "This is the first study to explore the spatial pattern and multilevel analysis of anemia among WRA in Nepal using stringent cluster sampling of comprehensive nationally representative data. See the comments above. Consider revising the arguments. There are many other studies in Nepal that used the same dataset and conducted the multivariate analysis. Page 19 line 381: you should include malaria related factors such as mosquito nets ownership, use of mosquito net, etc. It should not be a limitation as variables are available in the dataset. Conclusion The conclusion should be improved and linked to the main findings. For example: multipronged nutritional, and non-nutritional anemia prevention is not clear. Basically, your conclusion should say what your study results mean in real practice. For example, in order to address anemia among WRA, interventions promoting women's education economic livelihoods should be enhanced. Just an example. You need to summarize your main findings and state what they mean to the programs working to address anemia.

REVIEWER	Hu, Maogui Institute of Geographic Sciences and Natural Resources Research CAS

REVIEW RETURNED	24-Dec-2020

GENERAL COMMENTS	Some comments about statistic method: Line 143, what is the adjustment method? Line 154, "< 0.05" is redundant and should be removed. The same in line 180. Line 175, it is unclear how the prevalence ratio was standardized. Lines 182 and 184, the phrases positive autocorrelation and negative autocorrelation might be incorrectly used. In spatial statistics, positive autocorrelation contains both "high-high" and "low-low" patterns, i.e. hot spot and cold spot respectively. Negative autocorrelation usually indicates "high-low" type pattern. Line 185, the reference [9] is not related to the method in the sentence, please check it. What method used to estimate the confidence interval of prevalence in the table 1?

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Dr. Abhishek Agarwal, The INCLEN Trust International
Comments to the Author:
The present article require following changes:
Comments: Technical:
Comments: a. Role of hormonal contraceptives is not clear (table and Text do not match)
AUTHORS: Thank you for these comments. We have revised the table in the manuscript. Indeed, our study found those women who were using hormonal contraceptives were less likely to be anaemic (aOR: 0.63, 95% CI: 0.43-0.90). The details of interpretation have been presented in the discussion section.
Comments: b. The present study reflects the demographic variations between the different geographical areas which has association with anemia, so nothing new to be learn from the study.
AUTHORS: Thank you for your concern. This study aimed to explore the factors affecting anemia among women of reproductive age (WRA) in Nepal using spatial and multilevel epidemiological analysis. However, several studies have explored the factors associated with anemia among women of reproductive age (WRA) in Nepal which implies identifying the determinants of anemia only using multivariate analysis, but little is known about the demographic variations between the different geographical areas so far. Therefore, we believed the results of this study presented according to multilevel analysis and spatial patterns would be of great interest to the Nepalese government, policymakers, stakeholders, and researchers.
Grammatical
Comments: a. The spelling of anaemia or anemia are different at some places.
AUTHORS: We have replaced the word anemia with "anaemia" within the revised manuscript.
Comments: b. There is a need to rephrase the line 76 - 80 as the rationale and objective is not clearly reflected.
AUTHORS: Thank you for your suggestions. We have rephrased this sentence accordingly in the revised manuscript. Line: 42-43; page: 2

Reviewer: 2
Dr. Dieudonne Hakizimana, University of Global Health Equity
Comments to the Author:
The authors are addressing an important public health problem. The manuscript is well written but still needs improvement. The detailed comments are in the attached document.
General: the authors need to be consistent: either use anemia or anaemia (please revise the whole document)
AUTHORS: Thank you for pointing this out. We have replaced the word anemia with “anaemia” within the revised manuscript.
Abstract:
Comments: Well written and clear. In the conclusion, multipronged approaches are not specific, the authors should consider using a clear term.
AUTHORS: We thank the reviewers for the suggestion. We wanted to use the term “multi-pronged” approaches to state the several aspects that should be taken to control and prevent anemia. Now, we have revised the sentence accordingly to make it clearer.
Strengths and limitations of this study:
Comments: It is better the author mention also other qualitative factors not collected in DHS were not included in the study.
AUTHORS: Thank you very much for your suggestions. We have mentioned accordingly.
Background:
Comments: P5 line 56. For clarity, authors can separate the paragraph and mention the country first [in Nepal, …]. It gives the impression that it is a continuation of the previous information.
AUTHORS: We highly appreciate your thorough review. We have divided the paragraph as you suggested.
Comments: P6 line 76: the paragraph discussed the uniqueness of the study including using spatial analysis, identify factors associated with anemia using cluster sampling of nationally representative data. Some of the arguments are not correct. There are many studies that explored the factors associated with anemia in Nepal using the DHS data with national representation and collected using cluster sampling (the same data used in this study). Here are some examples:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6561639/
https://onlinelibrary.wiley.com/doi/full/10.1111/mcn.13044
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0236449
AUTHORS: Please allow us to partially agree with you that the only Gautam S. et al. (2019) article was published at the time of drafting this manuscript. However, Gautam S. et al. (2019) have explored the factors associated with anemia among women of reproductive age using multivariate analysis, but not spatial analysis. On 6th July 2021, Rai A. et al. published the paper using the multilevel epidemiological analysis. At that time, we already submitted our manuscript. In this paper, we used combined statistical methods including multilevel and spatial analysis, which takes into account the role of geographical risk profile and determinants of anaemia among WRA in Nepal which has not yet been explored in the Nepalese context. Considering your kind suggestions, we have now revised the sentence in the revised manuscript.
Comments: The authors should discuss other studies that used the same data and justify what is unique in this study. Probably showing geographic variation with spatial analysis and why it is important. Moreover, the study does not show the factors influencing anemia by geographic region as it claims here. The study just describes the prevalence of anemia by geographic region. The results show the factors at the national level as it is in other studies. The author should justify why this study is important compared to the other mentioned above as they are using the same data.
AUTHORS: A similar study have explored the spatial distribution and determining factors of anemia conducted by Kibret KT el. (2018)[1], Ejigu BA et al. (2018)[2], and Liyew AM et al. (2020)[3] in Ethiopia, and Lover AA et al. (2013)[4] in Timor-Leste. In addition, population in Nepal has diverse characteristics in terms of their culture, ethnicity and geographical locations. Within the latitude of 193km (North to South), Nepal bears tropical/sub-tropical landscape on the south and temperate to

alpine in the North, with an elevation ranging from 70m to the summit of Mount Everest (8848m)[38]. The distinct characteristics such as dietary habit, lifestyle and socio-economic status linked to the geographical regions of Nepal are unique and pose risk of developing anemia. Therefore, the spatial analysis of this study explores the geographical risk profile and determinants of anaemia among WRA in Nepal. We have mentioned these sentences in the revised manuscript. Line: 80-94; page: 5
Method
Comments: The author should give a description of the study setting for a better understanding of the context and the situation in the country.
AUTHORS: We have added the description of the study setting in the revised manuscript. Line: 107-110; page: 6
Comments: PAGE 6 Line 89: Not sure if the ERA is an abbreviation. If it is, it is used for the first time and should be written in full.
AUTHORS: Thank you for the suggestions. The New ERA is not an abbreviation. It is written as “New ERA” which is a private and non-profit research organization located in Kathmandu, Nepal.
Comments: Pa7 line 100 -103. The authors stated: .. women with available data on anemia…. were eligible for the survey. It is not clear if the author is describing the normal DHS sampling procedures as shown in figure 1 or the individuals included in the analysis for this study. The anemia is tested on a subset of the selected women. Women are not included in the study based on anemia data availability. The author should clarify if here they are describing the inclusion criteria for their analysis of the DHS sampling procedure and ensure they describe clearly.
AUTHORS: Thank you for pointing this out. We have deleted the sentence “available data on anaemia” to make clearer in the revised manuscript.
Comments: Moreover, Figure 1 describes the DHS data collection procedure for anemia. It is not adding much information as this study did not collect the data. The author should use the figure to describe their procedures in including individuals available in DHS dataset in their analysis if they excluded any and the exclusion criteria rather than describing the DHS procedure in the figure.
AUTHORS: Thank you very much for your insightful comments for highlighting sample size selection process in the methods section. Since we intended to assess the prevalence and factor associated with anaemia among WRA in Nepal using multilevel and spatial epidemiological model, this study required complete information of the WRA from the NDHS data files. The reproductive-aged women data are included in the IR file which contains all the data collected among the reproductive-aged women and sociodemographic variables of the household. For our study purpose, we used IR file for the analysis. Thus, we have now rephrased the sentence as “the details of the sample size selection in the NDHS 2016 are presented under Figure 1” in the revised manuscript. Line: 117-118; page: 7
Comments: P8 line 133: the authors mention: the mean value was used as a cut-off point of the proportion values for the categorization of community-level variables. The authors need to specify that it is only for the variables they calculated as it is not applicable to the province, residence.
AUTHORS: We agree with your comments. Based on the normal and not normal distribution of the aggregate variable (normal or non-normal), mean and median were used as a cut-off point for the categorization of community-level variables respectively. However, this procedure was not applicable for two variables such as place of residence and province. We have revised the sentence in the revised manuscript. Line: 148; page: 8

Comments: The use of the mean as the cut off for community female education and community wealth index should be justified. The cut off used influence the findings. Was the decision of using the mean an expert opinion or there is a standard? If the authors are comparing people below the mean and above the mean, it is likely that those below the mean will be likely different from those above. The use of mean as cut off should be justified with evidences.
AUTHORS: Thank you for the comment. If the aggregate variable was normally distributed, we calculated mean value and if not normally distributed median value was used as a cut off point for the categorization of community-level variables such as community female education, community wealth

index, source of drinking water and type of toilet facility. The various studies have already used similar type of model building to create a community-level variables for the multilevel analysis [5–7].
Comments: Page 9 line 142. The sentence: “Data were adjusted for enumeration areas (EAs) and disproportionate sampling and non-response” is not clear. If the authors would like to mention they adjusted for the effects of the stratification and cluster sampling approaches used in DHS, they should explicitly mention that. It is not clear how enumeration areas and non-response-response were adjusted in this study. DHS researchers have already taken care of that in calculating the survey weights.
AUTHORS: Thank you. We have revised the statement "The ‘svy’ command was used to account for sampling weights, clustering, and stratification in complex survey data" in the revised version of the manuscript. Line: 159-161; page: 8

Comments: In the results, the authors mention using the Pearson Chi-Square test for categorical variables and independent t-test for continuous variables, but this is not mentioned in the analysis section.
AUTHORS: Thank you very much for pointing this out. We have added the sentence as “Pearson Chi-Square test for categorical variables and independent t-test for continuous variables” in the statistical analysis section in the revised manuscript. Line: 162-163; page: 9

Spatial analysis
Comments: I am not very comfortable with Spatial statistical analysis; the editor should make sure they were appropriately used.
Comments: In the analysis, the author talked about calculating the standardized prevalence ratio. They should describe in details how they calculated the prevalence ratio to help readers who will want to replicate the same study.
AUTHORS: Thank you for the suggestion. To estimate the standardized prevalence ratio (SPR; ratio of observed prevalence to expected prevalence)[8] of anaemia among WRA, we first determined the prevalence of anaemia for both districts and provinces. Each corresponding district and province wise prevalence rate of anaemia among WRA was multiplied by the national prevalence rate of 41% (normalized to the national prevalence of 41%). Lover AA et al. (2014) also used the similar procedure to estimate the standardized prevalence ratio [9]. We have added these sentences in the revised manuscript. Line: 193-197; page: 10

S1 Table Plan for data coding and description of the study variables
Comments: For recoding the current contraceptive use variable, the authors separated the not using with natural/barrier and permanent methods. There should be a justification for this. Physiologically, the two are not different in terms of the likelihood of having anemia.
AUTHORS: Thank you for pointing this out. We have re-categorized the variable current contraceptive use as 1=Not using; 2=Hormonal; 3=Female sterilization; 4=Male contraception; 5= Traditional. These revised data are presented in revised manuscript, and S1 table.
Comments: Minimum dietary diversity for women (MDD-W): Better to say met or not met
AUTHORS: We have replace the word “diverse” with “Met” and “not diverse” with “Not met” in the revised S1 Table and manuscript.
Comments: Province: There is a typo in 1=Provice
AUTHORS: Thank you for pointing this typo error. We have corrected it.
Comments: Why malaria-related variables were not included in the analysis while they are known to be among important risk factors for anemia? The authors are recommended to include these in the analysis.
AUTHORS: We totally agree with your queries that malaria is also a well-established risk factors for anaemia. Even though we had strongly intended to include the malaria-related variables in the manuscript, malaria-related variables have not been collected in the IR files except only one variable: have mosquitoes bed net for sleeping. On the other hand, malaria-related factors such as having

mosquito nets, insecticide-treated net (ITN), and use of mosquito net are included in the HR files. We have now added the variable "have mosquitoes bed net for sleeping" from the IR file in the revised table.

Results

Comments: Page 11 line 201: typo: missing “were” More than one third (38.1%) of the participants….

AUTHORS: We have added as “More than one third (38.1%) of the participants were from age group 15-24 years...” in the revised manuscript. Line: 221; page: 11

Comments: Page 12 line 215: “the higher cases of anemia” should use prevalence instead of cases.

AUTHORS: We have replaced the word “cases” with “prevalence” in the revised manuscript.

Comments: Page 12 line 216: add “among women”: The prevalence of anemia was more “among women” who…

AUTHORS: Thank you for the valuable suggestion. We have added “among women” accordingly in the revised manuscript.

Comments: The authors should be consistent when presenting the results. In some places, they are presenting percentages and the odds in others.

AUTHORS: Thank you for the comment. Many researchers have also used both percentage and odds ratio term while interpreting the regression analysis [1,10,11]. For instance, Rai A et al. presented the results "women aged 20–29 years compared with those aged 40–49 years were 1.33 times (95% CI [1.04, 1.72]), women with four or more children compared with no children.....Women using hormonal contraception were 39% (AOR 0.61, 95% CI [0.50, 0.76]) less likely to be anemic".

Comments: Page 13 line 250 – 245: Women who belonged to communities with a high percentage of wealthy households had 1.48 times higher (aOR=1.48, 95% CI: 1.21-1.80) odds of anemia compared to those coming from a low percentage of the wealthy household; and women residing in communities with a high percentage of community female education had 1.39 times higher (aOR=1.39, 95% CI: 1.15-1.68) odds of anemia compared to those coming from the communities with a low percentage of education. The information presented here is different from the results in table 2. It is the other way around. This is very key for this study. You should revise.

AUTHORS: Thank you very much for pointing this out in the manuscript. We have revised this results with “Women who belonged to communities with a low percentage of wealthy households had 1.48 times higher (aOR=1.48, 95% CI: 1.21-1.80) odds of anemia compared to those coming from a high percentage of the wealthy household; and women residing in communities with a low percentage of community female education had 1.39 times higher (aOR=1.39, 95% CI: 1.15-1.68) odds of anemia compared to those coming from the communities with a high percentage of education” in the revised manuscript.

Table 1:

Comments: Severe anemia, Moderate anemia, and Mild anemia should be in the prevalence of anemia column.

AUTHORS: Thank you for your concern. We assure you that if we present the mild, moderate and severe anemia in the row form it would be easier to understand to the readers and previous study have also reported in the row.

Comments: For the Hemoglobin level, mean (+SD), there is a p-value, but it is not clear what was being tested. Did the author test the mean between the anemic and non-anemic? If it is the case, the mean/SD for non-anemic should also be reported.

AUTHORS: Yes, we tested the mean between the anemic and not anemic. However, not anemic data were not present in the previous table. We have now added the “not anemic” data and the related statistics in the revised table.

Comments: Some of the provinces are named Province-1, Province-2, and Province-5. The author should use the province names if they are available. The country context would help to clarify that.

AUTHORS: This is the first NDHS 2016 survey after the country has undergone to the federal states. The federal-state consists of seven administrative provinces. The provinces of Nepal were formed on

20th September 2015 in accordance with schedule 4 of the constitution of Nepal. The seven provinces replaced the previous administrative system and the new structure has been formed through rearranging the 77 districts of Nepal. The Government of Nepal has named some provinces only such as province 3 (Bagmati province), province 4 (Gandaki province), province 6 (Karnali province), and province 7 (Sudurpashim province). The remaining three province i.e. province 1, province 2 and province 5 are yet to be named by Government of Nepal.
Comments: Some individuals were not included in the analysis for some variables. The N for 6,414 but for BMI (n=6411) and Source of drinking water (n=6084). Can the author provide justification?
AUTHORS: Thank you for the comments. The variables such as BMI (n=6411), source of drinking water (n=6084), type of toilet facility (n=6084), and MDD-W (n=1131) have only mentioned observation in the DHS dataset. Therefore, we could use only those observations in the analysis.
Discussion
Comments: The subtitle “Overall findings” should be removed. It is expected that you discuss all findings. It is not clear what the subtitle means here.
AUTHORS: Thank you for your suggestion. We have deleted the subtitle “Overall findings” in the revised manuscript.
Comments: The discussion starts well with reminding the main finding. The authors are recommended to replace “serious” with “important” public health problem. Serious seems to be informal in public health practice.
AUTHORS: We have replaced the word “serious” with “important” in the revised manuscript.
Comments: Page 15 line 289: the authors mention one of the reasons for the high prevalence of anemia in the Terai region is a possibility that WRA from the Terai region and high mountainous regions are more likely to be of a lower socioeconomic status and thus can afford less diversified diet compared to other provinces and districts. This is contrary to the findings of this study and other discussion arguments. The authors should revise the justification. In in this study, the middle-class families are at high risk of anemia compared to the poor class and MDD-W was not found to be a predicting factor. Moreover, in the discussion, the authors also mentioned that most of the Nepalese people consume iron-rich staple foods including cereal, grains, lentils, and animal source food regardless of wealth status.
AUTHORS: Thank you for your insightful comments. We have revised the sentences accordingly.
Comments: The authors also discuss malaria as one of the factors for anemia. It is not clear why the author did not include malaria-related variables in the analysis while they are collected in the DHS.
AUTHORS: Thank you for emphasizing this comment again. We believe that we have already addressed this comment based on the previous suggestion.
Comments: P16 line 317: corroborate may not be an appropriate term – consider revising and use common terms like “similar findings”.
AUTHORS: We have revised the word “corroborate” with “similar findings” in the revised manuscript.
Comments: P16 line 327: In this study, the prevalence of anemia was 32.3% in the poorest, 41.5% in poorer, 48.9% in middle, 43.4% in richer, and 35.9% in richest households. This should be in the results. It is not necessary to repeat the results in the discussion, just explain the results.
AUTHORS: We thank the reviewer for the suggestions. We have revised the sentence accordingly.
Comments: P16 line 333: this sentence challenges your study: “Future research is critical to explore the association of household economic status and anemia among WRA in Nepal.”. Economic status was studied here and adjusted in all models. Does it mean the authors don’t trust the study results and recommend studying it again?
AUTHORS: Thank you for your concern. Women belonging to poorer households are more likely to be anaemic compared to those living in middle or richer households in most of the countries.[1,12,13]. In contrast, our study reported that poorer Nepalese women were less likely to be anaemic. Thus, we wanted to recommend the prospective researchers to explore the association of household economic status and anemia among WRA in Nepal in order to replicate the study.

Comments: The arguments about why the women in the middle category are more likely to have anemia compared to the poorest are not clear and convincing. They need to be supplemented with major differences between those categories. The authors said most of the Nepalese people [including middle and poor] consume iron-rich staple foods including cereal, grains, lentils, and animal source food regardless of wealth status. Thus, they should have similar risks, which is not the case in this study.
AUTHORS: We have added more evidence in these regards in the revised manuscript. Line: 359-373; page: 18

Comments: P17 line 338: Relatively higher prevalence of anemia at a younger age could be because of lower dietary iron intake and the additional demand for iron to compensate for iron loss during menstruation. This contradicts the previous argument. Here you mention young people have lower dietary iron intake while in the previous paragraph you mentioned: most of the Nepalese people consume iron-rich staple foods including cereal, grains, lentils, and animal source food regardless of wealth status. The authors should make sure the arguments explaining the results are consistent.
AUTHORS: We thank the reviewer for the comment. Indeed, the discussed findings in these paragraphs are based on the association of anaemia with WRA and study found the prevalence of anaemia to be higher in older age (>35 years) compared to younger age (25-34 years). We have also deleted the sentence “most of the Nepalese people consume iron-rich staple foods including cereal, grains, lentils, and animal source food regardless of wealth status”. We have now revised these paragraphs in the revised manuscript.
Comments: P 18 line 343: consider revising the language: In this study, the use of hormonal contraceptive methods was less likely to be associated with anemia among WRA. It should be those using hormonal contraceptive were less like likely to be anemic or had lower odds of anemia.
AUTHORS: We thank the reviewer for suggestions. We have revised the sentences accordingly in the revised manuscript.
Comments: P 18 line 360: could be due to the fact that WRA from Province-2 are more likely to be of a lower socioeconomic status and are less likely to afford a diverse diet. This argument contracts the study findings. Those poorer are less likely to be anemic compared to the middle and MDDW was not a predicting factor to explain the differences. The authors should supplement the justifications.
AUTHORS: The present study found the women who came from Province-2 were more likely to be anaemic. Despite the various health and nutrition intervention program implemented across the country, the most recent NDHS report found the women from province number 2 are more likely to be of a lower socioeconomic status and consume a less diverse diet with an estimated 29% of minimum dietary diversity (MDD) compared to other provinces in Nepal[15]. Other evidence from Nepal also report that women in Province 2 have poor nutritional status [16]. Socioeconomic status and consuming less diversified diet is well established causes of increased burden of anaemia among WRA. As such, considering this evidence we have highlighted this point in the case of province 2.
Comments: P18 line 44: The authors should support this argument with evidence: “with increase knowledge, women may also reduce the intake of tea, coffee, and some spices which are known to inhibit iron absorption”. This argument is weak. Iron absorption is not the single risk factor for anemia. Moreover, you should also justify if communities with high tea, coffee, and spices consumption are at high risk of anemia.
AUTHORS: We thank the reviewer for comments. We have revised the sentences accordingly in the revised manuscript.
General comments on the discussion:
Comments: The authors discuss many factors that may explain variations in anemia prevalence and risk. However, the authors do not compare and contradict the results with other studies in other settings. Moreover, it is not clear if the factors discussed in explaining the findings are particularly prone in the discussed regions compared to other regions. The authors should mention/justify that and make a comparison. For example, if the authors say: the majority (90%) of the population from the Terai region rely on groundwater especially shallow tube well

for domestic purposes including drinking compared to XXX in the other region.
AUTHORS: We have revised the discussion section as per your suggestions where needed. However, we were constrained by word limit (words=4000) and sincerely acknowledge that the reporting should have been prioritized.
Comments: Another example is Higher arsenic concentration can inhibit haem iron metabolism and increase erythrocyte hemolysis. Yes, that is known but we don't know how prevalent the condition in the region is compared to others, to be a possible explanation of anemia differences. Those are is just examples I picked from the discussion. The authors should revise their discussion and make comparisons throughout the discussion. Additionally, the authors should discuss the implications in terms of interventions in addressing anemia. For example, those with no education are at risk of anemia. And then what? How policy makers should use that information from the study? Which interventions should be put in place to address that considering the study findings?
AUTHORS: Thank you for your insightful comments. Considering your suggestions and comments, we have made necessary changes in the revised manuscript.
Strengths and limitation
Comments: Page 19 line 372: "This is the first study to explore the spatial pattern and multilevel analysis of anemia among WRA in Nepal using stringent cluster sampling of comprehensive nationally representative data. See the comments above. Consider revising the arguments. There are many other studies in Nepal that used the same dataset and conducted the multivariate analysis.
AUTHORS: We have revised this sentence with "This study is conducted based on the spatial pattern and multilevel epidemiological analysis of anemia among WRA in Nepal using stringent cluster sampling of comprehensive nationally representative data" in the revised manuscript.
Comments: Page 19 line 381: you should include malaria related factors such as mosquito nets ownership, use of mosquito net, etc. It should not be a limitation as variables are available in the dataset.
AUTHORS: We believe that we have already addressed this comment above. In addition, we have deleted the word "malaria" in the revised manuscript.
Conclusion
Comments: The conclusion should be improved and linked to the main findings. For example: multipronged nutritional, and non-nutritional anemia prevention is not clear. Basically, your conclusion should say what your study results mean in real practice. For example, in order to address anemia among WRA, interventions promoting women's education economic livelihoods should be enhanced. Just an example. You need to summarize your main findings and state what they mean to the programs working to address anemia.
AUTHORS: We have revised the conclusion section accordingly
Reviewer: 3
Dr. Maogui Hu, Institute of Geographic Sciences and Natural Resources Research CAS
Comments to the Author:
Some comments about statistic method:
Comments: Line 143, what is the adjustment method?
AUTHORS: Thank you very much for the comments. We have revised the statement "The svy commands have used that account for sampling weights, clustering, and stratification in complex survey data" in the revised version of the manuscript.
Comments: Line 154, "< 0.05" is redundant and should be removed. The same in line 180.
AUTHORS: W thank the reviewers for the comments. We have removed p-value <0.05 in the revised manuscript.
Comments: Line 175, it is unclear how the prevalence ratio was standardized.
AUTHORS: Thank you for your concerns. To estimate the standardized prevalence ratio (SPR; ratio of observed prevalence to expected prevalence)[8] of anaemia among WRA, we first determined the prevalence of anaemia for both districts and provinces. Each corresponding district and province wise

prevalence rate of anaemia among WRA was multiplied by the national prevalence rate of 41% (normalized to the national prevalence of 41%). Lover AA et al. (2014) also used the similar procedure to estimate the standardized prevalence ratio [9]. Line: 193-197; page: 10
Comments: Lines 182 and 184, the phrases positive autocorrelation and negative autocorrelation might be incorrectly used. In spatial statistics, positive autocorrelation contains both “high-high” and “low-low” patterns, i.e. hot spot and cold spot respectively. Negative autocorrelation usually indicates “high-low” type pattern.
AUTHORS: Thank you very much for your insightful comments. We have revised the sentences as “The Local Moran’s I, Gettis-Ord G-statistics tool in ArcGIS software was used to compute to measure how spatial autocorrelation of anemia among WRA varies across different locations in Nepal. The Getis-Ord G-statistics identifies statistically significant spatial clusters of hotspot clusters (High-High), and cold spot clusters (Low-Low).[3,17] Hotspot analysis computes Z-score and p-value to determine the statistical significance of the clustering of anemia over the study area at different significance levels simultaneously. [3,18] The statistical significance of autocorrelation was determined by z-scores and p-value ≤0.05 with a 95% Confidence Intervals (CIs).[1,18]” in the revised manuscript. Line: 198-205; page: 10

Comments: Line 185, the reference [9] is not related to the method in the sentence, please check it.
AUTHORS: Thank you for pointing this out. We have revised the reference here.

Comments: What method used to estimate the confidence interval of prevalence in the table 1?
AUTHORS: Thank you for the comment. In order to calculate the prevalence estimates and CIs, we used weighted cases for all the data to make representative of the entire population (pooled prevalence estimates) using 'svyset' command in Stata software. Subsequently, we analyzed the pooled prevalence and 95% CIs for each country. The similar command was used to calculate the pooled prevalence by Moschovis PP, et al [19].

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VERSION 2 – REVIEW

REVIEWER	Dr. Maogui Hu Institute of Geographic Sciences and Natural Resources Research, Chinese Academy of Sciences China
REVIEW RETURNED	30-Jan-2021

GENERAL COMMENTS	Thanks, I have no more comment.

REVIEWER	Dieudonne Hakizimana University of Global Health Equity (UGHE) Rwanda
REVIEW RETURNED	28-Feb-2021

GENERAL COMMENTS	The authors addressed the comments and the manuscript is ready for publication.