Author’s response to reviews

Title: An outline of anemia among adolescent girls in Bangladesh: findings from a cross-sectional study

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Author’s response to reviews:

Editor Comments:

1. We were unable to access the data you provided as part of the supplementary files. Can you please provide this in a different file format so that it can be accessed?

Response: The data has been provided in a different file format (.sav) as suggested

2. Confirm if written informed consent was obtained and where participants are minors (children) please confirm if assent was obtained from them and the written informed consent obtained from their parents/guardians

Response: We revised a sentence in Ethics approval and consent to participate section to address this issue. The revised sentence is “The purpose of the study was described to both the girls and
their parents. Verbal consent were obtained from both the girls and their parents, while written consent were given by the parents prior to the interview and the blood test.”

Reviewer 1 Comments:

1. Line 55-56 (and abstract): "anemia represents the status of both poor nutrition and poor health." Suggest revision here. It is simply low hemoglobin concentration and has many different causes not only related to poor nutrition and health.

Response: We revised the sentence as suggested. The revised sentence is “Anemia can be an indicator of low hemoglobin concentration in blood and represents both poor nutrition and poor health among many other things”

2. Line 57: "It is defined as a common blood disorders in which number and size of red blood cells…” Suggest revision here. It is not related to size of RBCs.

Response: We revised the sentence and re-written as “It is defined as a common blood disorders in which number of red blood cells, or the hemoglobin (Hb) concentration, falls below an established cut-off value, consequently impairing the capacity of the blood to transport oxygen around the body”

3. Line 65: "It primarily results from iron deficiency". Perhaps refer to a paper by Merrill et al. in Bangladesh indicating a very low prevalence of IDA: https://www.ncbi.nlm.nih.gov/pubmed/22705433


4. Line 72: What do the authors mean by "acquired hemoglobin disorders"

Response: The term acquired hemoglobin disorders have been elaborated and written as follows:

“Some genetic or acquired hemoglobin disorders caused by inherited mutations of the globin genes leading to qualitative and quantitative abnormalities of globin synthesis (sickle-cell disease
and thalassemia) also increases the risk for anemia, mainly in Mediterranean and Southeast Asian countries.”

5. Line 72-73: Would benefit reader to indicate how prevalent these genetic disorders are in Bangladesh.

Response: To indicate prevalence of acquired hemoglobin disorder caused by genetic disorders the following information is added with appropriate citation:

“In Bangladesh more than 7000 children born each year with thalassemia and WHO report estimates that there are about 3% beta-thalassemia carrier and about 4% HB E/beta-thalassemia carrier in Bangladesh [1].”

6. Line 75: Regarding reference 12 - this reference to Kaur et al appears incorrect as this paper refers to the impact of nutrition education on nutrition adequacy in the diet. Please double check if this is the one you mean to refer to.

Response: New reference [14] added instead of previous one:


7. Line 76: Same comment regarding reference 13 - is this the correct citation?

Response: New reference [15] added instead of previous one:


8. Line 97: “Carbohydrate based diet”. Do the authors mean a lack of iron rich animal sources in the diet? Otherwise I am not sure what they are referring to.

Response: Yes, this is correct. The lines are revised now as follows to make it clearer: “Other studies revealed the causal factors of anemia such consumption of traditional carbohydrate based diet lacking iron rich animal products…”
9. Line 101-2: Would deter from stating this is the first study of its kind that studied anemia among adolescents in Bangladesh. Please remove.

Response: Suggested lines have been removed from the manuscript.

10. Lines 103-4: The ability to "provide direction about the future public health interventions" is very limited from the data generated in this study.

Response: Revision has now been made to that line and it appears to the revised version as: “This study will shed light on not only the number of adolescents suffering from low blood hemoglobin level but also will provide information on the factors associated with it.”

11. Lines 109-116. It is not clear how sampling was conducted. Were adolescent girls randomly selected? Were numbers from each province/district proportionate-to-size? What proportion of girls refused to participate? Is this data generalizable to the larger population - at this point it is impossible to tell? Figure 1 is also not helpful as is.

Response: Now we have amended this paragraph and added the following lines to clarify your queries: “In the base survey, the sample was drawn from 21 equally divided clusters encompassing the entire country, of which 7 clusters were randomly selected for the present study. Thus, we opt to select all the adolescent girls (1467) from the selected households of 7 clusters as participants of the present study. However, we were unable to reach 10% of them due to unavailability and 1,314 adolescent girls were finally selected.”

12. Lines 134-135: "Considering the fact that the respondents were female, we recruited experienced female field enumerators for data collection to minimize bias". Please support this statement with a citation.

Response: We added the following reference after the sentence “considering the fact that the respondents were female, we recruited experienced female field enumerators for data collection to minimize bias [27]


13. Lines 143-48. It is completely unclear how the PCA was conducted to determine wealth index - what socioeconomic variables were used? What method? Is it valid?
Response: We followed a valid method i.e., used on several occasion to construct the wealth index as suggested in the cited reference (Gwatkin et al., 2007), and used a number of indicators i.e., household characteristics and asset attainment (similar to that of Bangladesh Demographic and Health Survey).

14. Line 151: Is it venous blood? I would assume capillary blood would be collected from a finger prick.
Response: Line is revised as suggested and rewrite as “Capillary blood was collected from all participants through pricking the fingertips by lancet”

15. Line 153: "hemoglobin (the iron carrying part of the blood cell)" …. Should this read oxygen-carrying rather?
Response: Yes. The line is rewritten as “A separate lancet was used for each individual and hemoglobin (the oxygen carrying part of the blood cell) concentration”

16. Line 154: What model of Hemocue? How many hemocues in total? Were Quality controls used? How were enumerators trained on blood collection?
Response: The information are now added to text as follows: “…..Hemocue portable hemoglobinometer (B-Hemoglobin Photometer, HemoCue AB, Angelhom, Sweden). A total of 7 machines were used and the enumerators were trained by a physician on the procedure and aseptic techniques. Researchers frequently visited the field and rechecked a number of adolescent girls for their Hb concentration to validate the enumerators’ activities.”

17. Lines 150: Hematological assessment: were any areas of the survey at an elevation above 1,000 meters? Was altitude taken into consideration in Hb assessment? What about smoking - is it common among Bangladeshi adolescents?
Response: All the selected areas for the survey were plain land. Due to cultural norms adolescent girls very rarely smoke in Bangladesh.

18. Line 167: I have never seen the acronym BAZ for BMI-for-age. Is this standard?
Response: Yes. BMI-for-age Z-score (BAZ) also called BMI standard deviation (s.d.) scores is WHO standard for adolescent girls [32].


19. Line 174-9: Why was Hb not assessed as a continuous variable? It would have been more rigorous? What other variables were included for the adjusted model? How were they included in the model?

Response: We categorized the Hb variable based on our objectives using established cut-off to classify the population into Anemic and non-Anemic. And for this WHO cut-off point was used for classifying severity of anemia [28] The other included variables for adjusting were described in Table 1 and Table 2 using appropriate cut-offs.

20. Line 180: No need for an equation for this regression.

Response: The equation is now omitted and the model building strategy is described as:

“Simple logistic regression (also called single covariate logistic regression) model was employed to analyze the potential risk factors for anemia among adolescent girls and crude odds ratio (COR) with 95% confidence interval (CI) were calculated. We followed the model building strategy as described by Akaike (1973) where the multiple logistic regression model with smallest Akaike Information Criteria (AIC) value considered as the best model.” [33]


21. Table 1: Were the pregnant women consuming IFA tablets at the time of hemoglobin assessment?

Response: Yes. We therefore, added the following sentences in the paragraph for additional information: “Moreover, 20 of the 45 currently pregnant women were consuming Iron and Folic Acid (IFA) supplement tablets.”

22. Table 1: Percentage could be presented with no decimal places, or one at the most.
Response: We revised all decimal points in the manuscript and considered only one decimal point.

23. Lines 202-18: Here many comparisons are made suggesting Hb was 'higher' or lower' in different groups - were statistical tests conducted to know if these were significant differences? For example: Line 213 indicates anemia was "slightly higher" among girls in 'slums as compared to rural areas' -53% vs. 51%.

P-values are added accordingly. For example, (53% versus 51%,) is written as (53% versus 51%, p-vale=0.589).

24. Lines 220-1: Hb 110.1 +- 11.5 g/dl. I assume you mean g/L here?? Same for the other two values reported.

Response: We revised g/dl in all cases and rewrite as g/L.

25. Table 2: This table presents way to much unnecessary data. Usually you would only present AOR for anemic women (no need to present each of the OR for each binary predictor either).

Response: We deleted the “not anemic” column and hence shown results only for “anemic” group with corresponding Chi-square value and p-value.

26. Table 2: Did you exclude pregnant women from the BMI-for-age assessment (not indicated for use in pregnant females)

Response: We included non-pregnant adolescent girls for BMI-for-age analysis

27. Table 3: would be helpful to include in the table (as footnotes even) what variables were used for adjustments.

Response: We considered age variable for adjustment and now mentioned as footnote accordingly.
28. Lines 242-3: Many other variables exist that are associated with anemia were not assessed in this model - parity, presence of inflammation or disease, other micronutrients, etc. Should be noted.

Response: Yes, this is a limitation of our study and has been discussed in the final paragraph of discussion section.

29. Figure 2 is not needed - adds no additional information that the text.

Response: We deleted Figure 2.

30. Discussion: overall is repetitive about anemia prevalence. Could be shortened by 2/3 and focused on the results on hand. Remove the assumptions from the discussion - lines 303-4 and 306-8.

Response: Suggested lines have been removed from the manuscript.

31. Line 310: If there was a "rigorous sampling method" it needs to be further detailed.

Response: Line is revised as suggested and rewrite as: “It followed a multistage cluster sampling procedure covering a wide region of both rural and urban areas and is generable to the entire population.”

32. Lines 311-2: "blood hemoglobin level is the most effective method of measuring anemia" - Sure, but there are limitations to the use of HemoCue as a device (as compared to hematology analyzers that use venous blood).

Response: We totally agree with you. Yet, this is more cost-effective measure compared to the hematology analyzer for community assessment. However, we revise the sentence as follows: “The biochemical procedure of testing blood hemoglobin level to ascertain anemia is one of the most effective methods of measuring anemia at community setting compared to other methods such as clinical examination.”

33. Lines 313-5: Unclear what the advantage is here please clarify or remove.
Response: We tried to rephrase and make the statement clearer in the following manner: “Another advantage is as it is a community based study it provides a population level assessment of anemia prevalence especially severe anemia, which is unlikely to be detected through school-based studies where only school going adolescent are available.”

34. Lines 322-3: Other research has showed very low IDA prevalence in Bangladesh, e.g. Merrill et al. mentioned earlier.

Response: Now, added a line addressing the issue: “However, other research reported a low prevalence of iron deficiency anemia among Bangladeshi women, most of them above the age of adolescence.”

35. Lines 335-7. Difficult to make these conclusions about policy change – when you actually do not know WHY women are anemic. Suggest to mention that more work is needed to determine the cause of anemia in these adolescent girls to determine what effective interventions are warranted.

Response: We revised the sentence and make changes as suggested. We added the followings: “Further studies regarding these issues would enhance our understanding and therefore more work is needed to determine the cause of anemia among adolescent girls to determine what effective interventions are warranted”

Reviewer 2 Comments:

This paper describes a cross-sectional study to assess the prevalence of anaemia in adolescent girls in Bangladesh and investigate social and reproductive status risk factors along with protein energy malnutrition, correctly using BMI-for-age z-score. The manuscript is sometimes lacking in clarity and there are errors in presentation of the data, but overall the methods are appropriate and basic interpretations of the statistical results correct. The results could be a little more critically discussed considering the somewhat surprising finding that pregnancy was protective for anemia.

General Comments:

1. From the methods, it appears that the sample was selected to be representative of the Bangladeshi population of adolescent girls. Can more details be provided (or reference made to a publically available protocol for the "multistage, cluster sampled, nationally
representative cross-sectional survey" (p6 lines 109-110) from which this study population was drawn? For example, only 15% of the sample were designated as "urban" is this representative of Bangladesh? According to World Bank country data it was 34% in 2015. How was the sample size of 1,314 arrived at for this sub-study? On what basis were the 1314 girls selected from the 4,536 adolescent girls in the main survey households?

Response: Now we have amended the first paragraph of methods and added the following lines to clarify your queries: “In the base survey, the sample was drawn from 21 equally divided clusters encompassing the entire country, of which 7 clusters were randomly selected for the present study. Thus, we opt to select all the adolescent girls (1467) from the selected households of 7 clusters as participants of the present study. However, we were unable to reach 10% of them due to unavailability and 1,314 adolescent girls were finally selected.”

Abstract: Minor Comments.

1. Lines 44-48. Suggest rewriting - don't include repeat the covariates for which you report the AOR in the text here. Were any of the co-variates included in models "a priori"?

Response: Rephrased the lines as per the suggestion and it appears: “After controlling for relevant covariates in multiple logistic regression model….”

2. Line 47 - Define "poverty" in the text as 1.54 is the AOR of the bottom wealth quintile compared to the richest quintile.

Response: Rephrased the lines as per the suggestion and it appears as: “……non-pregnancy (AOR: 6.10, 95% CI = 2.70-13.78, p-value <0.001), and households with bottom wealth quintile (AOR: 1.54, 95%CI = 1.03-2.30, p-value = 0.037) were identified as significant risk demographic factors of anemia among adolescent girls of Bangladesh.”

Introduction: Minor Comments:

1. Line 65. Suggest rewording to "though anemia has multifaceted etiology, the most common contributing factor is iron deficiency". Otherwise it reads as if you are suggesting that iron deficiency is the distal cause of all anemia, even if other factors are also involved.

Response: We changed the lines as suggested. Now we rewrite as: “Though anemia has multifaceted etiology, the most common contributing factor is iron deficiency”
2. Line 72 - SCD is most common in Africa. Are any of these inherited disorders common in Bangladesh?

Response: Yes, Thalassemia is common in Bangladesh. According to World health Organization (WHO), there are about 3% beta-thalassemia carrier and about 4% Hb E/beta-thalassemia carrier in Bangladesh. [13]


3. Lines 77-81. Are there any studies that suggest that cognitive defects in iron deficient adolescents or adults can be reversed by iron supplementation/improvement in anemia?

Response: Yes, we found a meta-analysis on the role of iron supplementation on cognition. We added a line within this paragraph as follows: “Several studies reported that iron supplementation among anemic adolescents and women had a role in cognition.”


Methods: Minor Comments:

1. Lines 113-114 The text reads to suggest that all the adolescents in the survey were mothers of children under 5, revise to improve clarity.

Response: We have amended the following lines to clarify your queries: “In the base survey, the sample was drawn from 21 equally divided clusters encompassing the entire country, of which 7 clusters were randomly selected for the present study. Thus, we opt to select all the adolescent girls (1467) from the selected households of 7 clusters as participants of the present study. However, we were unable to reach 10% of them due to unavailability and 1,314 adolescent girls were finally selected.”

2. Line 122 - what version of ODK was used? What is meant by “7” android?

Response: We corrected the line as per your suggestion as follows: “The entire data was collected electronically using ODK (Open Data Kit version 2.0)....”
3. Lines 125-140 - Was ODK being used offline during data collection or online. If offline, how often was data uploaded? Where was the ODK server hosted and who maintained it? Can you give any specific examples of how the QC checks and data validation?

Response: We address your queries and added a line to the text as follows: “The ODK was used in offline during the data collection and the questionnaires were uploaded every evening. The ODK server was hosted at the Head Office and was maintained by an experienced ICT person. To ensure accuracy of information of such a large dataset, a number of quality control measures were undertaken at different stages of the data collection procedure. For example, a researcher statistician was position at the head office to check the live data and to provide feedback thereby.”

4. Lines 151 - finger prick is "capillary" blood - not venous.

Response: Line is revised as suggested and rewrite as “Capillary blood was collected from all participants through pricking the fingertips by lancet”

5. Line 163 - "stadiometer"? Make? Or were these made locally by local artisans? If so - How were different ones compared to ensure measurements were similar across research teams?

Response: Yes, it was locally prepared and all the machines were checked several times and with similar subjects to validate the machine before using.

6. Lines 174-180 - were any variables included a-priori in multivar models? What criteria was used for including variables in multivar model, what strategy was used in model building?

Response: No, we did not incorporate any variable as priori in multivar model.

We described the model building strategy described by Akaike (1973) where the multiple logistic regression model with smallest Akaike Information Criteria (AIC) value considered as the best model.

7. Lines 180-184 - not necessary to show the equation for multivariable logistic regression.

Response: We omit the regression equation.
Results: Major Comment

1. Tables 2. It is more appropriate to present the percentages as column percentages. For example, present the proportion of girls who were currently married for the anemic and non-anemic groups = 251/678 = 37% vs. 252/636 = 39%.

Response: We thought that since our outcome of interest is anemia it is more meaningful to present particular characteristics among anemic adolescent girls. We also excluded the non-anemic cases from the table to make it more clarified.

Results: Minor Comments:

1. Why was pregnancy set as the baseline value for comparison in logistic regression? Pregnancy was quite rare and it would be more normal to use non-pregnancy as the baseline and compare the effect of pregnancy compared to non-pregnancy.

Response: We revised the reference category and now set non-pregnancy as the baseline value while running the logistic regression.

2. Table 2 - the numbers of currently pregnant in the non-anemic group add up to more than the total number in this group.

Response: The value was rechecked and corrected accordingly.

3. Table 2 - the starts indicating the range of p-values are not required as the actual values are presented. Note - do not report p=0.000, report the actual value or <0.001 or <0.0001 as per author guidelines.

Response: We rewrite all p-values where p-value less than 0.001 were written as <0.001.

4. Lines 227-231 - rewrite the text more concisely. Don't repeat all the results in the text that are in the tables.

Response: Lines 227-243 were rewritten:

“In simple logistic regression analyses, malnutrition and pregnancy status were significantly associated with anemia among adolescent girls (Table 3). The crude odds ratio (COR) for malnutrition status with anemia is found as 1.5 with p-value 0.052 where the 95% confidence
interval was found as (1.0, 2.2). Likewise, the COR for non-pregnancy compared to pregnancy status with anemia was found 0.2 with p-value <0.001 where the 95% confidence interval was (0.1-0.4).

However, after adjusting for potential covariates such as age, wealth index, marital status, regional effect and food security in multiple logistic model, malnutrition remained as an independent risk factors for anemia. Indeed, a malnourished adolescent girl had 40% more chance of anemia than a non-malnourished girl. It was also found that a pregnant adolescent girl had 5 times less chance of anemia compare to a pregnant girl. On the other hand, adolescent girls hailing from poorest or second poorest households were 50% more prone to become anemic compared to those from richest households. Besides, other covariates such as marital status, region and household food security status did not show any significant association with anemia status among adolescent girls.”

5. Lines 234-5 - interpreting an OR of 1.42 as increasing the risk by 42% is not quite correct. This is only true for risk ratios. The odds are increased by 42%.

Response: The interpretation was revised and written as: “a malnourished adolescent girl had 40% more chance of anemia than a non-malnourished girl”

6. Table 3 and results text for multivariable logistic regression results - see previous comments about model building and how and what co-variates were included in the final model. No results presented for age, literacy? I would suggest age should be included "a priori" and as a continuous variable in years.

Response: Now we considered the age variable for adjustment.

Discussion: Minor Comments:

1. Line 252 - "the prevalence of all form (sic) of anemia were found (51.6%), most of them (45.97%) were mildly anemic …" rewrite as:

Response: Rewritten as “While, the prevalence of all form of anemia were found 51.6%, most of them (46%) were mildly anemic and few (5.4%) were moderate with only 0.23% severely anemic”
2. "mild anaemia was the most common at 46% of the study population, with only 5.4% moderately anemic and 0.23% severely anemic. Can you see the difference in these sentences? The first suggests that only 46% of the anemic cases were mildly anemic!

Response: Rewritten as suggested as: “mild anemia was the most common at 46% of the study population, with only 5.4% moderately anemic and 0.23% severely anemia”

3. Line 258 – in the DHS anemia data quoted – who were the study population?

Response: Now the information about the study population has been added in the lines: “Prevalence of anemia reported in our study was similarly high to the most recent Bangladesh Demographic and Health Survey (BDHS) where the prevalence of any form anemia were 48.6%, while mild, moderate and severe anemia were 39.2%, 9.4% and 0.0% respectively among adolescent girls of 15-19 years ”

4. Lines 270-78 –Critically evaluate this study in comparison to the other studies – Ref No 32? Comparable or not? Sample size?

Response: The reference has been removed from the text now as you have suggested that it is not comparable to the current context of the study

5. Lines 300-308 -The prevalence of pregnancy was quite low in this study population compared to the 31 % reported in ref [40]. Was any data collected on if the girls had ever been pregnant? Or were breast-feeding?

Response: Our study only encompasses currently pregnant and non-pregnant adolescent girls.