

## PEER REVIEW HISTORY

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

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Sex differences in prevalence and determinants of hypertension among adults: a cross-sectional survey of one rural village in Bangladesh
<b>AUTHORS</b>	Islam, Jessica; Zaman, M Mostafa; Ahmed, Jasim; Choudhury, Soheli Reza; Khan, Hasanuzzaman; Zissin, Tashfin

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Hyeon Chang Kim Yonsei University, Korea
<b>REVIEW RETURNED</b>	26-Feb-2020

<b>GENERAL COMMENTS</b>	<p>The study reports the prevalence and risk factors of hypertension/pre-hypertension in a rural community in Bangladesh. This study is of interest in the study area. However, there are some limitations.</p> <p>First of all, this study is based on a single community. Unless this region represents Bangladesh's entire population or entire rural population, the results of the study are difficult to make sense outside the region. It is unclear why the study was conducted in this area.</p> <p>The authors mentioned that younger study population (18 years old or older) as the novelty of this study. However, there are several studies from Bangladesh, targeting people over 20, 25 and 35 years old. A little expansion of the target age group is not an important uniqueness.</p> <p>The reported prevalence of hypertension is much lower than prevalence from other previous studies. The authors also mentioned this and explained the reasons in two ways. The first interpretation is that the study subjects are younger than in other studies. However, when comparing by age group, the study's hypertension prevalence is much lower also in middle-aged and elderly people compared to other studies. Therefore, it is difficult to interpret that the difference in prevalence is due to the age difference of those studied. The second explanation is that it would be the effect of the public health intervention in the study region. For this explanation to be valid, it should show whether the public health interventions in this area are different from other regions and, consequently, the distributions of hypertension risk factors are different from other regions. I did not find other data, but compared BMI distribution of this study with those from others. The study population does not seem to have lower obesity rates compared with others. A more plausible explanation is needed for the very low prevalence of hypertension in this study.</p>
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	<p>It is also an unusual finding that there is no one with hypertension among 18 to 29 years of age. If the prevalence rate is so low, it would be better to present the distribution of systolic and diastolic blood pressures and compare it with other studies, rather than just reporting the prevalence of hypertension.</p> <p>Salt intake seems to have been assessed by the amount of salt added to the cooked food. I doubt that this method can properly reflect excessive sodium intakes.</p>
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<b>REVIEWER</b>	Dr Sunil Kumar Singh North Delhi Municipal Corporation Medical College and Hindu Rao Hospital, Delhi, India
<b>REVIEW RETURNED</b>	04-Mar-2020

<b>GENERAL COMMENTS</b>	<p><b>Title</b></p> <ol style="list-style-type: none"> <li>1. In the title, you should include the name of study population that whether it is adults or adolescent or geriatric.</li> <li>2. You should use the word “associated factors” instead of “risk factors” in the title.</li> <li>3. You can use only hypertension word instead of both prehypertension and hypertension. As hypertension will include both.</li> <li>4. You should use word “rural area” instead “rural district”</li> </ol> <p><b>Abstract</b></p> <ol style="list-style-type: none"> <li>1. You can't use short forms (CVD) without using its full form before.</li> <li>2. You can reframe the sentences in settings and participants. For example, A cross sectional study was planned in which a total of 2600 adult men and women from a rural area of Bangladesh, were included in the study over period of 12 months. Data on sociodemographic characteristics, physical measurement, blood pressure, behaviour factors and health history was collected from all participants. Data was analysed by Stata/SE 15.1</li> <li>3. You should write prevalence of hypertension was instead of hypertension prevalence everywhere.</li> <li>4. Mean age and sex distribution of participants should be mentioned in the abstract.</li> <li>5. You should not use word “may be” in conclusion in the first line.</li> </ol> <p><b>Introduction</b></p> <ol style="list-style-type: none"> <li>1. You should not write that “we assessed” in the introduction. You should write in the form of objectives of your research at the end of introduction. (127-128).</li> </ol> <p><b>Materials and methods</b></p>
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	<ol style="list-style-type: none"> <li>2. It is unclear that this study is based on secondary data analysis or it is a cross sectional study as you have mentioned in line 137 that data for analysis was obtained through routine ECOH's surveillance.</li> <li>3. Kindly check on WHO step questionnaire definitions, to label a person as hypertensive according to WHO step questionnaire, we should take three reading and average of last two reading should be taken. We should take a fourth reading after four weeks for those people who came to be in prehypertensive or hypertensive category during first visit.</li> <li>4. You should mention the definition of past and current smoker and alcoholic as it is clearly mentioned in STEPS questionnaire.</li> </ol> <p><b>Results</b></p> <ol style="list-style-type: none"> <li>1. Response rate at individual level is 58.9% only. (You can follow sampling method at household level after calculation of sample size to increase the response rate in future studies).</li> <li>2. In line 237 and 238, you have used word majority for 38.3% , you can write about one-third of participants instead of word majority.</li> <li>3. You can write word "majority" for 58% in line 276.</li> </ol> <p><b>Discussion</b></p> <ol style="list-style-type: none"> <li>1. Kindly check the definition of uncontrolled hypertension. You have mentioned in 312 and 313 that those who are unaware of their hypertensive condition will have more uncontrolled hypertension. I think uncontrolled hypertension word is used if hypertension is not controlled on medication.</li> <li>2. You can make discussion a little short as few results are mentioned repeatedly.</li> </ol> <p><b>Conclusion</b></p> <ol style="list-style-type: none"> <li>1. You didn't mention about the second objective of your study that what were the common associated factors you have found in your study.</li> <li>2. You can add some more recommendations from your study.</li> </ol>
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<b>REVIEWER</b>	Anbrasi Edward Johns Hopkins University, USA
<b>REVIEW RETURNED</b>	18-Mar-2020

<b>GENERAL COMMENTS</b>	A well designed study addressing a key public health priority, describing sex based disparities for sex-specific interventions. Inclusion of participants >18y, provides additional rationale for strategies to address pre-hypertensives. The discussion section can be further strengthened by providing more information on current or proposed national or ECOH strategies for prevention and mgt of the disease. A well written paper.
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## VERSION 1 – AUTHOR RESPONSE

### Reviewer 1 Comments:

Comment: First of all, this study is based on a single community. Unless this region represents Bangladesh's entire population or entire rural population, the results of the study are difficult to make sense outside the region. It is unclear why the study was conducted in this area.

Response: Thank you for your inquiry. In the village where the study was conducted, Dr. M. Zaman (2nd author) is the founder of a health center called the Ekhlaspur Center of Health or ECOH. This center conducts routine data collection from the area for monitoring and evaluation of the burden of chronic disease. As such, data are available to evaluate trends in chronic disease prevalence and identify differences across demographic groups for public health program prioritization. While this rural village may not be representative of the nation, 64% of the population remains rural and factors such as access to healthcare and healthcare infrastructure are consistent across rural areas of Bangladesh. We believe these data provide evidence that may be reflective of other rural areas. Finally, as governmental funding for research is limited, we believe utilizing available data for research is necessary for low and middle income countries.

To address the reviewer's concern, we have added the following to the Limitations section: "Our study is limited to one rural area of Bangladesh and may not be reflective of other areas of the country."

Comment: The authors mentioned that younger study population (18 years old or older) as the novelty of this study. However, there are several studies from Bangladesh, targeting people over 20, 25 and 35 years old. A little expansion of the target age group is not an important uniqueness.

Response: Thank you. The World Health Organization has developed a Global Monitoring Framework ([https://www.who.int/nmh/global\\_monitoring\\_framework/en/](https://www.who.int/nmh/global_monitoring_framework/en/)) to monitor progress of noncommunicable disease control. One of the 25 indicators is the "age-standardized prevalence of raised blood pressure among persons aged 18+ years." We believe this paper provides data, which can be used to inform this indicator as Bangladesh prepares an update on its progress by 2025. Please find link here: [https://www.who.int/nmh/global\\_monitoring\\_framework/2013-11-06-who-dc-c268-whp-gap-ncds-techdoc-def3.pdf?ua=1](https://www.who.int/nmh/global_monitoring_framework/2013-11-06-who-dc-c268-whp-gap-ncds-techdoc-def3.pdf?ua=1).

We have included this point in the strengths section of the Discussion. However, to address the reviewer's concern, we have replaced the first strength of the article listed to as follows: "The population studied was enumerated by the Ekhlaspur Center of Health (ECOH) study staff, which allowed us to provide accurate estimates of prevalence using a well-defined denominator in a rural area of Bangladesh."

Comment: The reported prevalence of hypertension is much lower than prevalence from other previous studies. The authors also mentioned this and explained the reasons in two ways. The first interpretation is that the study subjects are younger than in other studies. However, when comparing by age group, the study's hypertension prevalence is much lower also in middle-aged and elderly people compared to other studies. Therefore, it is difficult to interpret that the difference in prevalence is due to the age difference of those studied. The second explanation is that it would be the effect of the public health intervention in the study region. For this explanation to be valid, it should show whether the public health interventions in this area are different from other regions and, consequently, the distributions of hypertension risk factors are different from other regions. I did not find other data,

but compared BMI distribution of this study with those from others. The study population does not seem to have lower obesity rates compared with others. A more plausible explanation is needed for the very low prevalence of hypertension in this study.

Response: Thank you for your inquiry. We believe our population's low prevalence of hyperglycemia is an important confirmatory factor that shows our population may be generally healthier than other rural areas. In the Fottrell et al 2018 BMJ Global Health paper of over 12,000 rural adults, they found the prevalence of hyperglycemia was 17.2% in men and 23.4% in women<sup>1</sup>, which is much lower than what we observed (3.2% among women and 2.2% among men). Important public health interventions that we were unable to measure are fruit and vegetable consumption, and physical activity, which may be attributable to the lower prevalence of high blood pressure and hyperglycemia.

While the authors understand the reviewer's concern, we believe the importance of free and accessible preventive services should not be overlooked. As we describe in our paper, "ECOH has provided hypertension treatment services for several years. The clinic provides patients with counselling on lifestyle changes and provides antihypertensive medications free of charge." This is substantively different than other rural areas of Bangladesh. In 2014, an estimated 16% of health care facilities across the country (i.e. hospitals, community clinics) had the resources to diagnose, prescribe treatment for, and manage patients with hypertension and other CVDs<sup>2</sup>. District hospitals (95%), Upazila health complexes (81%), and private hospitals (77%), which are only found in urban areas, were more likely to provide services for cardiovascular diseases than other facilities. Only 10% of community clinics and maternal and child welfare centers, and 17% of union level facilities, which are the most accessible providers in rural areas, provided any cardiovascular services, and the services at these facilities are limited to the measurement of blood pressure or referrals<sup>2</sup>. We believe that our findings are reflective of what can be achieved in other areas of Bangladesh.

We have updated the Discussion to improve the clarity of our argument and clarify that we believe this difference in prevalence of hypertension and other NCD risk factors is due to access to care.

Comment: It is also an unusual finding that there is no one with hypertension among 18 to 29 years of age. If the prevalence rate is so low, it would be better to present the distribution of systolic and diastolic blood pressures and compare it with other studies, rather than just reporting the prevalence of hypertension.

Response: Thank you. While the prevalence of hypertension is low, we would like to bring attention to the fact that the prevalence of prehypertension in this age group is quite high (men: 29% and women 26%). However, to address the reviewers concerns we have included a Figure of SBP and DBP distribution by age group and sex, now labeled as Figure 1.

Comment: Salt intake seems to have been assessed by the amount of salt added to the cooked food. I doubt that this method can properly reflect excessive sodium intakes.

Response: Thank you for your comment. Salt intake has been defined as "additional salt added to every meal after it has been cooked" in prior studies conducted in low and middle-income countries<sup>3</sup>, including a recent NCD survey published in BMJ Global Health<sup>1</sup>. This is because studies have shown in developed countries, processed foods contribute the most to salt consumption, while in some LMICs, the evidence shows that salt added at the table (i.e. additional salt added to every meal) or while cooking largely contributes to the amount of salt intake for that population<sup>4 5</sup>.

#### Reviewer 2 Comments:

Comment: In the title, you should include the name of study population that whether it is adults or adolescent or geriatric. You should use the word "associated factors" instead of "risk factors" in the title. You can use only hypertension word instead of both prehypertension and hypertension As

hypertension will include both. You should use word “rural area” instead “rural district”

Response: Thank you. We have updated the title as follows: “Sex differences in prevalence and determinants of hypertension among adults: a cross-sectional survey of one rural village in Bangladesh.”

Comment: You can't use short forms (CVD) without using its full form before.

Response: Thank you. This has been updated.

Comment: You can reframe the sentences in settings and participants. For example, A cross sectional study was planned in which a total of 2600 adult men and women from a rural area of Bangladesh, were included in the study over period of 12 months. Data on sociodemographic characteristics, physical measurement, blood pressure, behavior factors and health history was collected from all participants. Data was analysed by Stata/SE 15.1

Response: Thank you for your comment. You are recommending we change the writing style from active voice to passive voice. This is a stylistic choice. Please see link below. For clarity, the authors prefer to maintain active voice. ([https://cgi.duke.edu/web/sciwriting/index.php?action=passive\\_voice](https://cgi.duke.edu/web/sciwriting/index.php?action=passive_voice))

Comment: You should write prevalence of hypertension was instead of hypertension prevalence everywhere.

Response: Thank you for your comment. It is common practice to use the verbiage “hypertension prevalence.” The authors provide several examples:

- “Hypertension Prevalence and Control Among Adults: United States, 2011-2014.” <https://www.ncbi.nlm.nih.gov/pubmed/26633197>
- “Diabetes and hypertension prevalence in homeless adults in the United States: a systematic review and meta-analysis.” <https://www.ncbi.nlm.nih.gov/pubmed/25521899>
- “Hypertension Prevalence Jointly Influenced by Acculturation and Gender in US Immigrant Groups.” <https://www.ncbi.nlm.nih.gov/pubmed/30165394>
- “Hypertension Prevalence, Awareness, Treatment, and Control Among Adults Aged  $\geq 18$  Years - Los Angeles County, 1999-2006 and 2007-2014.” <https://www.ncbi.nlm.nih.gov/pubmed/28817553>
- “Hypertension prevalence and blood pressure levels in 6 European countries, Canada, and the United States.” <https://www.ncbi.nlm.nih.gov/pubmed/12746359>

Comment: Mean age and sex distribution of participants should be mentioned in the abstract.

Response: Thank you. The following sentence has been added to the abstract: “The average age of participants was 41.6 years and 53.7% were women.”

Comment: You should not use word “may be” in conclusion in the first line.

Response: Thank you. We have changed “may be” to “is.”

Comment: You should not write that “we assessed” in the introduction. You should write in the form of objectives of your research at the end of introduction. (127-128).

Response: Thank you. We have removed “we assessed” and update the sentence as follows: Our objective was to evaluate differences in prevalence and associated determinants of hypertension and

prehypertension in a rural area of Bangladesh.

Comment: It is unclear that this study is based on secondary data analysis or it is a cross sectional study as you have mentioned in line 137 that data for analysis was obtained through routine ECOH's surveillance.

Response: The study is both as these phrases are not independent. It is a cross-sectional study because the data were collected during one specific time frame 2014-2015. And the presented paper is a secondary data analysis as the data were collected for routine surveillance. We have updated the Abstract to clarify.

Comment: Kindly check on WHO step questionnaire definitions, to label a person as hypertensive according to WHO step questionnaire, we should take three reading and average of last two reading should be taken. We should take a fourth reading after four weeks for those people who came to be in prehypertensive or hypertensive category during first visit.

Response: Thank you for this point. We are aware of the WHO questionnaire definitions as Dr. Zaman was the prior World Health Organization Country Office for Bangladesh's National Non-Communicable Disease Program Officer. He ensured that his staff followed the WHO's recommendations. We have updated the text to clarify that a test run was completed for blood pressure readings prior to the final two readings. We have included the following in the limitations: "Additionally, we did not repeat blood pressure readings after 4 weeks to confirm a diagnosis of hypertension."

Comment: You should mention the definition of past and current smoker and alcoholic as it is clearly mentioned in STEPS questionnaire.

Response: Thank you. We did not include questions on alcohol use in this study and it is not presented in the tables. We have included the following in the text: "We defined past tobacco users as respondents who were ever users of tobacco, however, currently do not use tobacco products." [https://www.who.int/tobacco/surveillance/en\\_tfi\\_tqs.pdf](https://www.who.int/tobacco/surveillance/en_tfi_tqs.pdf) (page 4)

Comment: In line 237 and 238, you have used word majority for 38.3% , you can write about onethird of participants instead of word majority.

Response: Thank you. We have updated to say About one-third.

Comment: Kindly check the definition of uncontrolled hypertension. You have mentioned in 312 and 313 that those who are unaware of their hypertensive condition will have more uncontrolled hypertension. I think uncontrolled hypertension word is used if hypertension is not controlled on medication.

Response: Thank you. We agree and have removed this line.

Comment: You can make discussion a little short as few results are mentioned repeatedly.

Response: Thank you. We agree and have edited the Discussion.

Comment: You didn't mention about the second objective of your study that what were the common associated factors you have found in your study.

Response: Thank you. We included the following in the Discussion on determinants of hypertension:

In our analysis, we found that female sex, older age, higher education, high BMI and blood glucose

levels approaching the diabetic range ( $\geq 11.1$ ) were determinants of hypertension, which is similar to prior nationally-representative studies conducted in Bangladesh 6-8. These determinants were consistent across sex groups, excluding educational status. Among men, higher education led to an increase in hypertension prevalence when compared to no education. However, among women, higher education appeared to have a protective effect when compared to no education although not statistically significant after adjustment. Higher educational attainment among women may be lead to employment, higher physical activity and active commuting, which have been shown to reduce sedentary behavior among Bangladeshi women 9.

Comment: You can add some more recommendations from your study.

Response: Thank you. We have added some recommendations to the Discussion.

Reviewer 3 Comments:

Comment: A well designed study addressing a key public health priority, describing sex based disparities for sex-specific interventions. Inclusion of participants >18y, provides additional rationale for strategies to address pre-hypertensives. The discussion section can be further strengthened by providing more information on current or proposed national or ECOH strategies for prevention and mgt of the disease. A well written paper.

Response: Thank you for your kind comments. We have included the following to address this comment: "Published in 2013, the Guidelines for Management of Hypertension in Bangladesh largely recommend and focus on lifestyle measures to reduce the risk of hypertension in adults<sup>10</sup>. This is because Bangladesh is a low resource setting with limited availability of trained health care providers and treatment, particularly in rural areas. Affordability of treatment is an important factor all providers should consider, since costs may impact adherence and continuity of care. In our setting, we observe a low prevalence of hypertension, particularly among younger groups, and also hyperglycemia. We believe this low prevalence is due to the availability and access to preventive health care, such as physical activity and tobacco cessation campaigns. We recommend that other rural areas follow the national guidelines for hypertension management, and promote similar lifestyle changes, to achieve similar burden reduction."

1. Fottrell E, Ahmed N, Shaha SK, et al. Distribution of diabetes, hypertension and non-communicable disease risk factors among adults in rural Bangladesh: a cross-sectional survey. *BMJ Glob Health* 2018;3(6):e000787. doi: 10.1136/bmjgh-2018-000787
2. NIPORT. Bangladesh Health Facility Survey 2014 Dhaka, Bangladesh: National Institute of Population Research and Training (NIPORT), Associates for Community and Population Research (ACPR), and ICF International. ; 2016 [Available from: <https://dhsprogram.com/pubs/pdf/SPA23/SPA23.pdf> accessed 03/15 2019.
3. Sookram C, Munodawafa D, Phori PM, et al. WHO's supported interventions on salt intake reduction in the sub-Saharan Africa region. *Cardiovasc Diagn Ther* 2015;5(3):186-90. doi: 10.3978/j.issn.2223-3652.2015.04.04
4. WHO. Global status report on noncommunicable diseases Geneva World Health Organization; 2014 [Available from: [http://apps.who.int/iris/bitstream/10665/148114/1/9789241564854\\_eng.pdf?ua=12020](http://apps.who.int/iris/bitstream/10665/148114/1/9789241564854_eng.pdf?ua=12020).
5. Campbell NR, Neal BC, MacGregor GA. Interested in developing a national programme to reduce dietary salt? *Journal of human hypertension* 2011;25(12):705-10. doi: 10.1038/jhh.2011.25
6. Rahman M, Zaman MM, Islam JY, et al. Prevalence, treatment patterns, and risk factors of hypertension and pre-hypertension among Bangladeshi adults. *Journal of human hypertension* 2017 doi: 10.1038/s41371-017-0018-x



7. Chowdhury MA, Uddin MJ, Haque MR, et al. Hypertension among adults in Bangladesh: evidence from a national cross-sectional survey. *BMC cardiovascular disorders* 2016;16:22. doi: 10.1186/s12872-016-0197-3
8. Islam JY, Zaman MM, Haq SA, et al. Epidemiology of hypertension among Bangladeshi adults using the 2017 ACC/AHA Hypertension Clinical Practice Guidelines and Joint National Committee 7 Guidelines. *Journal of human hypertension* 2018;32(10):668-80. doi: 10.1038/s41371-018-0087-5
9. Moniruzzaman M, Mostafa Zaman M, Islalm MS, et al. Physical activity levels in Bangladeshi adults: results from STEPS survey 2010. *Public health* 2016;137:131-8. doi: 10.1016/j.puhe.2016.02.028
10. National Guidelines for Management of Hypertension in Bangladesh. Dhaka, Bangladesh: WHO/SEARO/Country Office for Bangladesh and DGHS, Ministry of Health and Family Welfare 2013.