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Journal Name:	British Journal of Medicine and Medical Research
Manuscript Number:	Ms_BJMMR_27559
Title of the Manuscript:	Interrelationship of serum uric acid levels and cardiovascular disease risk factors in Bangladeshi patients treated with antihypertensive drugs
Type of the Article	Original Research Article

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

(<http://www.sciencedomain.org/page.php?id=sdi-general-editorial-policy#Peer-Review-Guideline>)



SDI Review Form 1.6

PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Compulsory REVISION comments	<ul style="list-style-type: none"> -Better characterization of cases and controls (abstract line 12 “no serious disease” is not enough) -Did any subjects have previous CV events?? -It is quite surprising that women are more than men (generally more man than women with CV disease) - the sum is 197, not 200 -Revision for style and Typing errors -The authors did not consider gender as determinant in the statistical analysis, although it is well known that males have higher UA levels than females. -Glycemia as well was not considered -Also correct for EGRF -Show distribution of UA, and percentage ogf hyperuricemic subjects (according to which guidelines). Also discuss the issue of range to define hyperuricemia. - the text, especially the results section are written in a colloquial language, a bit of work to reflect a more professionally and schematic written manuscript. 	<p>Q1. Better characterization of cases and controls (abstract line 12 “no serious disease” is not enough).</p> <p><i>Answer:</i> Characterization has been included in the revised version, please see yellow-shaded area.</p> <p>A total number of 200 subjects were included in his study irrespectively of race, religion and socioeconomic status. Of the total, 40 subjects were healthy control, 59 were cardiovascular subjects (taking blood pressure-, and lipid-lowering drugs), and 98 were cardiovascular subjects (without taking blood pressure, and lipid-lowering drugs).</p> <p>Healthy control subjects were with no serious disease.</p> <p>Control subjects definition</p> <p>Healthy control subjects' health status was evaluated by the physicians after measurements of blood pressure, anthropometrics and laboratory parameters, including serum lipid profile, electrolyte elements such as Na, K, Cl, and micronutrient zinc (Zn) and uric acid. Healthy control subjects also were with no serious disease.</p> <p>Case definition</p> <p>High blood pressure (hypertension) is by far the most important risk factor for cardiovascular disease (CVD). Therefore, case subjects, who had cardiovascular-risk factors such as high blood pressure and high blood cholesterol, were defined by the presence of symptoms consistent with cardiac disease, such as, self-reporting complaints of persistent high pressure. Physicians re-evaluated the subjects' complaints by determining relevant parameters, as were done for control subjects. The participants were asked for whether they had already visited the doctors and started 'taking' of lipid-lowering- and anti-hypertensive drugs. Responders with 'no' were included and assigned as hypertensive subjects without drugs (WOD). On the other hand, if the subjects, with</p>



SDI Review Form 1.6

		<p>hypertension and high lipid profile, were already taking antihypertensive and lipid-lowering drugs, for at least 3-months, were included in the study and classified as hypertensive subjects with drugs, WD.</p> <p>Inclusion criteria The inclusion criteria for the control and CVD subjects was that the adult subjects must be aged ranging from 50 to 70 years.</p> <p>Exclusion criteria Subjects with diseases, such as infection, major surgery, renal failure, renal disease, liver malfunction and diabetes, history of using specific steroidal drugs and other pre-existing medical conditions or history of illegal drug use and crossing the age limit (40 to 70) were excluded from the study.</p> <p>Page 2, 58-75, and Page 3, lines 76-88.</p> <p>Q2. Did any subjects have previous CV events? Answer: Does it mean, whether did the subjects had suffered from heart attack, stroke etc? No, there were no such events.</p> <p>Q3. It is quite surprising that women are more than men (generally more man than women with CV disease) Answer: In our subjects without drugs (WOD), BMI, SBP were not different between male vs. female; however, DBP was lower in the female than the male. In the subjects with drugs (WD), there were no differences BMI, SBP and DBP between male vs. female subjects.</p> <p>Q4. the sum is 197, not 200 Answer: The number of subjects have been corrected to 197.</p> <p>Q5. Revision for style and Typing errors : Answer:</p>
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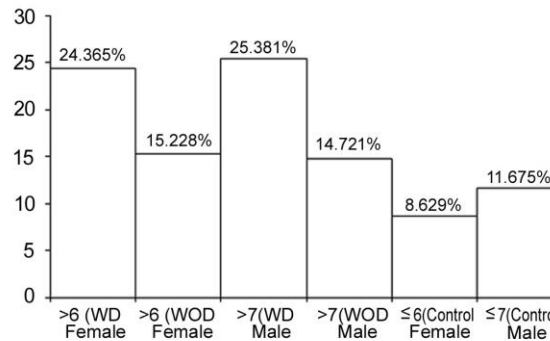
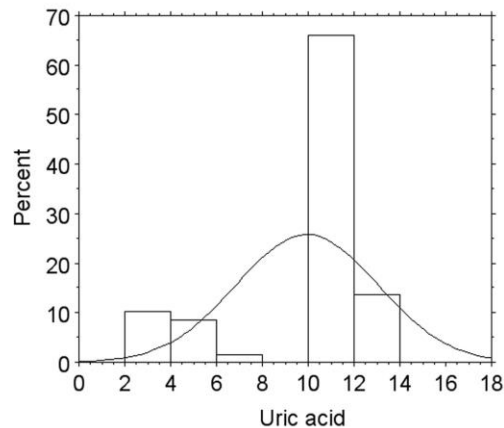
SDI Review Form 1.6

		<p>Style has been revised as per the journal. Typos have been corrected.</p> <p>O6. The authors did not consider gender as determinant in the statistical analysis, although it is well known that males have higher UA levels than females.</p> <p>Answer: In our investigation with 197 subjects, UA levels were not different between male vs. female subjects in the control group. The UA levels also were not different in the male vs. female both in the WOD or WD hypertensive subjects.</p> <p>Q7. Glycemia as well was not considered:</p> <p>Answer: In the exclusion criteria, you can see that we excluded the diabetic patients. We excluded the diabetic subjects in order to eliminate the confounding factors on the relation between uric acid vs. other cardiovascular disease risk factors.</p> <p>Q8. Also correct for EGRF</p> <p>Answer: We have corrected.</p> <p>Q9. Show distribution of UA, and percentage of hyperuricemic subjects (according to which guidelines). Also discuss the issue of range to define hyperuricemia.</p> <p>Answer: Please see the Figure below and descriptions.</p> <p>Q10. the text, especially the results section are written in a colloquial language, a bit of work to reflect a more professionally and schematic written manuscript.</p> <p>Answer: We have tried our best to improve the language.</p>
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SDI Review Form 1.6

<u>Minor</u> REVISION comments		
<u>Optional/General</u> comments		



Normal uric acid levels are 2.4~6.0 mg/dL (female) and 3.4~7.0 mg/dL (male) (<http://chemocare.com/chemotherapy/side-effects/hyperuricemia-high-uric-acid.aspx>). Abdullah et al (2015) recently reported the association of uric acid levels in 93 Bangladeshi patients with acute coronary syndrome (Abdullah AS, Begum N, Khan MAH, Hossain M, Kabir SMEJ, Alam MS, Chowdhury AW, KhanHILR. Admission Serum Uric Acid Levels and In-Hospital Outcomes in Patients with Acute Coronary Syndrome. J Enam Med Col 2015; 5(1): 15–22). In the report, serum uric acid concentrations >7 mg/dL in men and >6 mg/dL in women were assigned as hyperuricemic, while serum uric acid concentrations ≤7 mg/dL in men



SDI Review Form 1.6

and ≤ 6 mg/dL in women were assigned as normouricemia. If the same range is ascribed to the levels of our subjects, the following results were obtained in distribution analysis: Irrespective of sex, 20.30% subjects were normouricemic and 79.7% were hyperuricemic, among which 29.949% subjects were in the without drugs (WOD) group, while 49.746% were in the with drugs group (WD). If gender was included in the distribution analysis, we obtained the following results: Among the hyperuricemic subjects, 25.38% male subjects with drugs were hyperuricemic and 14.72% male subjects without drugs were hyperuricemic. Correspondingly, 24.36% female subjects with drugs (WD) were hyperuricemic, while 15.22% female subjects without drugs (WOD) were hyperuricemic.

Finally, we have added the following sentences:

Considering the serum uric acid concentrations >7 mg/dL in men and >6 mg/dL in women as hyperuricemia ; and ≤ 7 mg/dL in men and ≤ 6 mg/dL as normouricemia, 25.38% male subjects with drugs were hyperuricemic and 14.72% male subjects without drugs were hyperuricemic in our investigation. Correspondingly, 24.36% female subjects with drugs (WD) were hyperuricemic, while 15.22% female subjects without drugs (WOD) were hyperuricemic.

Page 4, Lines 144-149.