Reviewer's report

Title: the effect of tobacco, XPC, XPD and XPG genetic variants in bladder cancer development

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Reviewer: Dinesh Kumar Ahirwar

Reviewer's report:

The authors have described a study evaluating the effect of a subset of DNA repair gene polymorphisms on susceptibility to bladder cancer in association with tobacco smoke. There are several factors that need to be addressed before this manuscript is acceptable for publication.

Major compulsory revision:

1. There is no information on how authors calculated sample size for the study. Considering numbers of individuals recruited (193 patients and 193 controls) and a lower minor allele frequency of XPG (rs17655) polymorphism, it is really important to estimate whether current sample size successfully predict odds for bladder cancer incidence. The issue becomes more serious when data get stratified in sub-groups like smoking habits and sample size further reduces in the cells of a 2x2 table. Therefore, author should provide details of sample size calculation and should apply appropriate correction for small sample size, where required.

2. The recruitment criteria for controls is not clear, whether they were work out for absence of any urinary tract disease and confirmed by cytoscropy or by any other means is not clear.

3. Another major issue is correction for multiple comparisons. I think author may like to use Bonferroni’s correction when analyzing genotype and tobacco use or tumor stage. I guess, most of the marginal association will turn into non-significant association after this correction, which is a major lacuna of this study.

4. There are reports which suggest that patients with same stage of tumor but with different grade, behave differently to treatment and tumor invasion (Ref. Scand J Urol Nephrol. 2003;37(3):195-201). Therefore, following patient classification pattern, presented in that paper, according to stage and grade both, may provide some fruitful information.

5. Though they adjusted OR for age and gender, they have completely ignored presence or absence of smoking.

6. In most of the complex diseases such as bladder cancer, many genes are involved and they interact with each other to alter disease phenotype. Therefore,
analyzing combined effect of these polymorphisms would be interesting and useful.

Minor Essential Revisions
1. Page 20, par 2, line 7- “This results confirms…..” should be “These results confirm”.
2. “Smokers patients” should be replaced with smoker patients at all places.
3. There are many sentences need to be rephrased.
4. I would suggest following HUGO nomenclature through out the manuscript.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
'I declare that I have no competing interests'